POSTERS' SESSION

POSTERS' SESSION PS05
EXPERIMENTAL HYPERTENSION

PP.05.01 CALCIUM SENSITIZATION IN DAHL RATS: GENETIC PREDISPOSITION AND THE ROLE OF ENDOGENOUS VASOACTIVE SYSTEMS

J. Zicha, M. Behuliak, J. Kunes, I. Vaneckova.
Institute of Physiology AS CR, Prague, CZECH REPUBLIC

Objective: Salt hypertension in Dahl rats is characterized by attenuation of renin-angiotensin system (RAS), enhancement of sympathetic nervous system (SNS) and relative NO deficiency. The important role of enhanced calcium entry through L type voltage-dependent calcium channels (L-VDCC) in the development and maintenance of high blood pressure (BP) of salt hypertensive Dahl rats is well known, but less attention was paid to calcium sensitization mediated by RhoA/Rho kinase pathway in salt hypertension.

Design and method: Our study was aimed to determine calcium sensitization in salt-sensitive (DS) and salt-resistant (DR) Dahl rats fed either low-salt (LS, 0.3% NaCl) or high-salt diet (HS, 5% NaCl). Dose-dependent administration of Rho kinase inhibitor fasudil, calcium channel opener BAY K8644 or norepinephrine (NE) to rats with different state of endogenous vasoactive systems (RAS, SNS and/or NO) was used to reach this goal. BP response to fasudil administration and the impact of fasudil pretreatment on BP response to NE or BAY K8644 were performed in conscious animals in which endogenous vasoactive systems were intact or inhibited by captopril, pentolinium or L-NAME.

Results: Increasing fasudil doses caused greater BP reduction in DS than DR rats with intact endogenous vasoactive systems, the effect being prominent in DS-HS rats. If rats with combined inhibition of RAS and SNS were studied, fasudil pretreatment caused greater rightward shift of NE dose-response curve and larger attenuation of the magnitude of BAY K8644 dose-response curve in DS than DR rats, but these differences were not influenced by high salt intake in either strain. To clarify different BP response to fasudil in intact DS-LS and DS-HS rats, we also studied rats subjected to NO synthase blockade or to a combined RAS, SNS and NOS blockade. Acute NO-deficiency augmented fasudil-induced BP reduction in both strains but preserved the difference between DS-LS and DS-HS rats, which was almost abolished by additional RAS and SNS blockade.

Conclusions: Our data suggest that increased calcium sensitization in DS rats (due to a genetic predisposition) is further augmented by chronic high salt intake via enhanced SNS activity.

PP.05.02 CARDIAC (PRO)RENIN RECEPTOR EXPRESSION IS INCREASED IN HYPERTENSIVE RATS WITH AORTIC CONSTRICTION

Y. Zhang, L. Ma, B. Wang, J. Wu. *Taishan Medical University, Taian, CHINA*

Objective: (Pro)renin receptor ((P)RR), a specific receptor for renin and prorenin, was identified as a member of the renin-angiotensin system (RAS) by Nguyen et al. (P)RR is a 350 amino acid protein with a single transmembrane domain and is widely expressed in various tissues. While implicated in a broad range of diseases, studies to date have focused on the kidney. We sought to examine the expression of the (P)RR and its relationship with the expression of PLC-b3 in the heart in hypertensive rats induced by abdominal aortic constriction.

Design and method: Sixty SD rats were divided into 4 groups (n=15/group) as following: sham operated (SO), rats with the aortic constriction (AC), AC rats were given (P)RR inhibitor HRP (4μg kg-1 d-1, SC), and AC rats given PLC-b3 inhibitor U73122 (40μg kg-1 d-1, SC). MAP was recorded using a tail-cuff method. After 4 weeks of treatment, levels of (P)RR and PLC-b3 in the heart were examined by RT-PCR, western blot and immunohistochemistry. (Pro)renin activity (PRA) was measured by radioimmunoassay.

Results: The partial aortic ligation led to an increase in blood pressure and cardiac hypertrophy in rats. The expression level of (P)RR was significantly increased (1.5-fold, $P < 0.01$), and PLC-b3 also increased (1.8-fold, $P < 0.01$) in the left ventricle of the heart in hypertensive rats, compared with that in sham operated ones. There was a correlation between the expression of (P)RR and PLC-b3. Treatment of HRP significantly reduced the expression of (P)RR. Similarly, the level of PLC-b3 was suppressed in the heart with administration of U73122.

Conclusions: The enhanced expression of activated (P)RR was observed in the heart with hypertrophy inhypertensive rats that were aortic constricted, and the similar response of PLC-b3 obtained in the animal model. Both were markedly suppressed in the heart in rats treated with HRP and U73122, respectively. These results suggest that cardiac PLC-b3 may play a role in hypertension and cardiac hypertrophy induced by (P)RR.

PP.05.03 PLASMA ALDOSTERONE CONCENTRATION IS POSITIVELY CORRELATED WITH PULSE PRESSURE IN HYPERTENSIVE POPULATION

X. Yao, N.F. Li, Y.J. Zhang, A. Suofeiya, D.L. Zhang, G.J. Chang, K.M. Zhou, J. Hong.
The Center of Hypertension of the Peoples Hospital of Xinjiang Autonomous Region, Hypertension Institute of Xinjiang, Urmuqi, CHINA

Objective: There is increasing evidence of a link between vessel stiffness and pulse pressure (PP), in which plasma aldosterone concentration (PAC) may play a role. The study was performed to explore the potential relationships between plasma aldosterone concentration and pulse pressure in patients with hypertension.

Design and method: We evaluated the relationship between baseline pulse pressure, measured by 24-hour ambulatory monitoring blood pressure and plasma concentration of aldosterone in supine, seated and upright positions in 195 general hypertensives. They were divided in three groups by tertiles of PP: PP<=44mmHg (n=70), 44mmHg<PP<=51mmHg (n=63) and PP>=51mmHg(n=62). The PAC in different postures was compared respectively.

Results: (1) The baseline characteristics of the patients when segregated by tertiles of PP showed that statistically significant differences were found in K+ concentration, 24-hour Systolic blood pressure(BP), 24-hour diastolic BP, sex, upright PAC, and sitting PAC. (2) The levels of PAC were significantly different in 3 levels of PP groups whatever postures takes by multifactor ANOVA analysis, the individuals with PP>=51mmHg had the highest levels of PAC. On contrast, the subjects with higher baseline level of Ald (PAC>12ng/dl) showed greater PP than those with lower Ald (PAC<=12ng/dl). (3) Weak association between pulse pressure and upright (r=0.288, P<0.001), seated (r=0.265, P<0.001) and supine posture (r=0.191, P=0.008) respectively were detected by using simple correlation analysis. After corrected plasma potassium, age and sex, the partial correlation coefficients did not change greatly. (4) The Logistic regression model was constructed with PP>=40mmHg or PP<40mmHg as the dependent variable, the plasma potassium and Ald were included as contributing factors, in which the plasma Ald played a risk role [OR=0.025,95% CI:0.35(0.13-0.88)] in higher PP rather than the plasma potassium showed a protective factor[OR=0.043,95%CI:1.09(1.00-1.12)].

Conclusions: Although these data provide weak evidence for a link between pulse pressure, which is related to vessel stiffness, and plasma aldosterone concentration in general hypertensive patients, the PAC indicated to be a risk factor for higher pulse pressure.

PP.05.04 IS ATRIAL KICK REPRESENTS THE USEFUL INFORMATION FOR THE BAROREFLEX SENSITIVITY OF TOTAL ARTIFICIAL HEART (TAH)?

T. Yambe, H. Miura, Y. Shiraishi, T. Shiga. *Tohoku University, Sendai, JAPAN*

Objective: No one control the hypertension in TAH circulation.
In severe cases of the profound biventricular failure, heart transplantation and artificial heart have been the last option. However, the number of cases for transplantation had been limited not only in Japan, but also in the all over the world. Ventricular assist device has been the one of the most important therapeutic option. However, in severe biventricular failure, satisfactory therapeutic results could not be able to be obtained till now. TAH must be one of the last candidates.

In TAH circulation, no one control the hemodynamic condition, because there is no control center like human brain.
In this paper, we want to propose the new artificial baroreflex system to control the TAH based on the sinus mode rhythm.

Design and method: Six healthy adult goats were used in the experiments for the removal of the natural ventricles and implantation of the rotary blood pumps (Sun Medical, Suwa, Japan). After weaning the cardiopulmonary bypass, rotary blood pumps maintained the circulation under the condition of the atrial contraction restart without both ventricles.
In the system of the pneumatically driven TAH, both ventricles had been removed and driving ventricle would be implanted. So, surgical procedure of our TAH system is same.

Results: This surgical results had meant the TAH in the anatomical meaning. Furthermore, we can achieve the measurements of the atrial contraction due to the sinus rhythm. So, we can control the rotary blood pump control based on the information of the sinus node rhythm. Furthermore, the Rotation of blood pump can be controlled by the information of the blood pressure changes by our automatic control system.

Conclusions: Yes, we can achieve the artificial baroreflex system for TAH, because we can control the rotational speed of rotary blood pump by the use of the information of atrial kick.

PP.05.05 AEROBIC EXERCISE TRAINING IN HYPERTENSIVE RATS PROMOTES IMPORTANT CARDIAC MORPHOFUNCTIONAL ADAPTATIONS WITHOUT MODIFICATIONS IN BLOOD PRESSURE

S. Vieira, K. Delgado Maida, H. Celso Dutra De Souza
Medical School, University of São Paulo, Ribeirão Preto, BRAZIL

Objective: To investigate the relationship between hemodynamic morphological and functional cardiac adaptations resulting from aerobic physical training (APT) in young spontaneously hypertensive rats (SHR).

Design and method: Eighteen-week–old SHR (N=8) and Wistar-Kyoto (WK) (N=7) were submitted to APT by swimming for 10 weeks. Arterial blood pressure (BP) and heart rate (HR) were measured using the tail plethysmography; cardiac morphology and function were evaluated by means of 2-D echocardiography. All evaluations were performed before and after the period of the APT. Statistical analysis was done using Sigma-Stat® software. The values are presented as mean ± standard error of the mean. The Student's t-test was used, followed by the Mann-Whitney test when necessary. Ethics Committee on Animal Experiments (n. 092/2012).

Results: The APT promoted bradycardia in both groups (SHR and WK), however, it did not reduce the BP. The SHR group presented significant adjustments after the APT: increase in cardiac output (78.6 ml/min ± 8.5 vs. 110.50 ml/min ± 8.4; $p = 0.018$); in systolic volume (234.4 µl ± 23 vs. 323.9 µl ± 26.8; $p = 0.024$); and in the end-diastolic volume (384 µl ± 28.4 vs. 633 µl ± 31.5; $p < 0.001$). We also observed changes in cardiac morphology characterized by an increase in the diastolic area (81.6 mm² ± 4.1 vs. 111 mm² ± 3.3; $p < 0.001$) and in the systolic area (47 mm² ± 3.7 vs. 74.4 mm² ± 3.1; $p < 0.001$). In contrast, the WK group only had an increase in the end-diastolic diameter (7.6 mm ± 0.15 vs. 8.9 mm ± 0.52; $p= 0.049$), end-systolic diameter (4.4 mm ± 0.15 vs. 5.7 mm ± 0.54; $p = 0.037$) and in the shortening fraction (13.4 % ± 1.4 vs. 19.3 % ± 1.9; $p = 0.040$).

Conclusions: APT caused greater changes in the SHR group, mainly those related to functional variables. Also based on the literature, it was observed that, although this training protocol has not significantly reduced the SHR rats' blood pressure, it was effective in preventing the progress of hypertension between the 18th and 28th weeks of life.

PP.05.06 ATORVASTATIN, EPA AND DHA EXHIBIT ACUTE ANTIARRHYTHMIC EFFECTS AND FACILITATE TERMINATION OF VENTRICULAR FIBRILLATION IN HEREDITARY HYPERTRIGLYCERIDEMIC AND HYPERTENSIVE (HTG) RATS

C. Viczenczova [1], T. Benova [1], V. Knezl [2], J. Slezak [1], N. Tribulova [1]. *[1] Institute for Heart Research, Slovak Academy of Sciences, Bratislava, SLOVAK REPUBLIC, [2] Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences, Bratislava, SLOVAK REPUBLIC*

Objective: Statins and omega-3 FA (omega-3) exhibit antiarrhythmic effects in clinical practice but underlying mechanisms are not fully elucidated. We have previously shown that prolonged treatment of HTG rats with these compounds reduced the incidence of ventricular fibrillation (VF) that was attributed in part to modulation of cardiac cell-to-cell electrical coupling via connexin-43 channels. To elucidate further underlying antiarrhythmic mechanims this study was aimed to examine whether these compounds exert acute antiarrhythmic effects.

Design and method: Experiments were conducted on adult, male and female HTG rats known to be much prone to VF than healthy rats. The heart was excised from anesthetized rats and perfused with oxygenated Krebs-Henseleit solution at constant flow. VF inducibility was tested in control hearts and compared with the hearts, which were pre-treated during 10 min prior el. stimulation with either Atorvastatin, eicosapentanoic acid (EPA) or docosahexanoic acid (DHA) in concentration 1.5, 7, 15 µmol.

Results: Sustained VF was induced in all HTG rat hearts without treatment. In contrast, the hearts subjected to atorvastatin, EPA and DHA were less susceptible to inducible VF and incidence of sustained VF was reduced to 30%, 70% and 80% in male and to 60%, 75% and 60% in female rats. Atorvastatin suppressed VF inducibility in male rats already in concentration 1.5 µmol while EPA and DHA were efficient at higher 7 and 15 µmol. Moreover, bolus (150 µmol) of EPA and DHA administered directly to fibrillating heart terminated VF in 6 of 6 hearts and atorvastatin in 3 of 6 hearts.

Conclusions: Atorvastatin likewise EPA and DHA exhibit clear antifibrillating and defibrillating efficacy when acutely applied. This fact suggests that these compounds might affect directly connexin-43 channels and likely other channel function involved in arrhythmogenesis. Findings point out the importance of pleiotropic effects of statins and diet-related approaches in prevention of malignant arrhythmias.

PP.05.07 SIMILAR EFFECTS OF DIFFERENT CLASSES OF RAS-BLOCKING AGENTS ON PRINCIPAL VASOACTIVE SYSTEMS IN REN-2 TRANSGENIC RATS

I. Vaneckova, Z. Dobesova, J. Kunes, J. Zicha.
Institute of Physiology, Academy of Sciences, Prague, CZECH REPUBLIC

Objective: In humans, direct renin inhibitors were postulated to have higher effects on sympathetic nervous system than other classes of renin-angiotensin system (RAS) blockers. We were interested whether different classes of blockers of renin-angiotensin system vary in their effects on distinct vasoactive systems contributing to blood pressure (BP) maintenance in a model of angiotensin II-dependent hypertension, i.e. heterozygous Ren-2 transgenic rats (TGR).

Design and method: Young (5-week-old) male heterozygous TGR rats were given either angiotensin receptor blocker (ARB) losartan (10 mg/kg/day in the drinking fluid), angiotensin converting enzyme inhibitor (ACEi) captopril (20 mg/kg/day in the drinking fluid), or direct renin inhibitor (DRI) aliskiren (30 mg/kg/day via osmotic minipumps) for 4 weeks. BP was monitored with tail-cuff plethysmography (Hatterras). At the end of the study basal BP and acute responses to consecutive blockade of renin-angiotensin (RAS) (10 mg/kg captopril), sympathetic nervous (SNS) (5 mg/kg pentolinium), and nitric oxide (NO) (30 mg/kg L-NAME) systems were determined in conscious rats. Moreover, BP response to acute inhibition of nifedipine-sensitive calcium influx through voltage-dependent calcium channels was measured.

Results: All three classes of RAS inhibitors similarly decreased BP (122±6 mm Hg for aliskiren; 111±3 mm Hg for captopril and 114±2 mm Hg for losartan). The BP lowering effects of all three groups of RAS-blocking agents was achieved mainly via the attenuation of captopril-sensitive (RAS-dependent) vasoconstriction, the strongest effect being exerted by losartan. Sympathetic vasoconstriction was moderately reduced in all three treated groups of TGR rats with the lowest effect of losartan. NO-dependent vasodilation was similarly reduced in all three RAS-blocked groups. Moreover, calcium channel blockade with nifedipine normalized BP in all treated groups of TGR rats.

Conclusions: The effects of all three classes of RAS-blocking agents on principal vasoactive systems are comparable, with no beneficial effects of direct renin inhibitors.

PP.05.08 SUPPRESSION OF AUTOANTIBODY PRODUCTION TO BETA1-ADRENERGIC RECEPTOR BY OMEGA-3 FATTY ACIDS DEMONSTRATED IN EXPERIMENTAL HYPERTENSION

N. Tribulova [1], J. Radosinska [2], B. Bacova [1], G. Wallukat [3], V. Knezl [4], J. Zurmanova [5], T. Soukup [6], B. Barancik [1], J. Slezak [1]. *[1] Institute for Heart Research, SAS, Bratislava, SLOVAK REPUBLIC, [2] Faculty of Medicine CU, Dept. Physiology, Bratislava, SLOVAK REPUBLIC, [3] Max-Delbruck Centrum for Mol Medicine, Berlin, GERMANY, [4] Institute of Pharmacology and Toxicology, Bratislava, SLOVAK REPUBLIC, [5] Faculty of Science, Dept. Physiology, Prague, CZECH REPUBLIC, [6] Institute of Physiology, v.v.i. AS CR, Prague, CZECH REPUBLIC*

Objective: Autoantibody production to the adrenergic beta-1 receptors (b1-AAB) is known to contribute to development of dilated cardiomyopathy and arrhythmogenic substrate. Hypertension if not properly controlled is deleterious to health due to inflammation, myocardial remodelling and enhancement of b1-AAB. Numerous reports, including ours, indicate cardioprotective effects of omega-3 FA in condition when omega-3 index is low. We hypothesized that omega-3 intake may affect production of b1-AAB, myocardial remodelling and connexin-43 (Cx43) mediated electric cell-to-cell coupling in aged spontaneously hypertensive rats (SHR).

Design and method: Male and female 12-month-old SHR as well as their age-and-sex-matched healthy Wistar rats were used. Rats fed by standard laboratory chow were compared with those supplemented with pure omega-3 ethyl ester (200 mg/kg b.w. /day) for two months. Blood serum was used for the detection of b1-AAB. Expression of Cx43, myosin heavy chain (MyHC), activity of matrix metalloproteinase 2 (MMP2) and ultrastructure were examined in left ventricular tissue. Susceptibility to electrically-induced ventricular fibrillation (VF) was tested using Langendorff-perfused heart.

Results: Comparing to healthy rats, male and female SHR exhibited significant increase of serum levels of b1-AAB, activity of MMP2, shift of alpha to beta MyHC isoform, down-regulation and miss-localisation of Cx43 and subcellular injury of the cardiomyocytes. It was associated with higher incidence of VF. Omega-3 intake resulted in significant decrease of BP, b1-AAB levels and MMP2 activity in both male and female SHR. In addition, there was a clearcut increase of Cx43 mRNA and protein expression, partial elimination of Cx43 miss-localisation and preservation of subcellular integrity of cardiomyocytes and their junctions. MyHC profile was not affected by treatment either male or female SHR but incidence of VF was significantly reduced.

Conclusions: Suppression of beta1-adrenoceptors autoantibody production and extracellular MMP-2 activity is a novel mechanism implicated in cardioprotective effects of omega-3 fatty acids. It was linked with up-regulation of myocardial Cx43, improvement of cardiomyocytes integrity and protection from VF.

PP.05.09 OXIDATIVE STRESS AND VASCULAR DYSFUNCTION IN THE OFFSPRING OF PROTEIN-RESTRICTED HYPERTENSIVE RATS

K. Takemori [1], H. Ito [2]. *[1] Department of Food Science and Nutrition, Faculty of Agriculture, Kinki University, Nara, JAPAN, [2] Department of Biomedical Engineering, Faculty of Biology, Oriented Science and Technology, Kinki University, Wakayama, JAPAN*

Objective: It has already been revealed that protein restriction during pregnancy may affect health and diseases after birth (so-called DOHaD theory). Reactive oxygen species (ROS) may have an important role in the potential mechanism underlying the programming of hypertension in utero. However, it is still unclear how ROS may induce hypertension or vascular dysfunction in the offspring of protein-restricted dams. In this study, we investigated the effects of ROS on vascular function in the stroke-prone spontaneously hypertensive rats (SHRSP) offspring of protein-restricted dams.

Design and method: Male and female SHRSP offspring were obtained from dams fed either a control diet containing 20% casein or a protein-restricted diet containing 9% casein with pair feeding until gestation (control group and protein-restricted group, respectively). Oxidative stress was induced in 12-week-old offspring by administering phorbol 12-myristate 13-acetate (PMA; NADPH oxidase activator) by osmotic mini pump for 4 weeks. At 16 weeks of age, anti-oxidant enzyme activities in red blood cell fraction and plasma diacron-reactive oxygen metabolites (dROMs) contents were assessed. Using thoracic aorta, we investigated the vascular reactivity and the expression of endothelial nitric oxide synthase (eNOS) and soluble guanylic acid cyclase (sGC) by Western blot analysis.

Results: Although no significant differences were found in body weight of dams fed the protein-restricted or control diet, the birth weight of male and female offspring of the protein-restricted group was lower than that of the control group. No significant difference was found in blood pressure between the two groups. Plasma d-ROMs level was significantly higher in the protein-restricted group than in the control group, whereas anti-oxidant enzyme activities were similar in both groups. In the thoracic aorta, acetylcholine-induced relaxation was significantly reduced in the protein-restricted group. Expression of eNOS was lower and expression of sGC was higher in the protein-restricted group.

Conclusions: We conclude that protein restriction during pregnancy may induce hyper-sensitivity to oxidative stress and vascular dysfunction in SHRSP offspring. Thus, administration of antioxidant(s) may be useful to prevent or treat hypertensive vascular injury in mature offspring exposed to a poor intrauterine environment.

PP.05.10 TENASCIN-C MAY ACCELERATE CARDIAC FIBROSIS BY ACTIVATING MACROPHAGES VIA INTEGRIN ALPHAVBETA3 /NF-KAPPAB/IL-6 AXIS

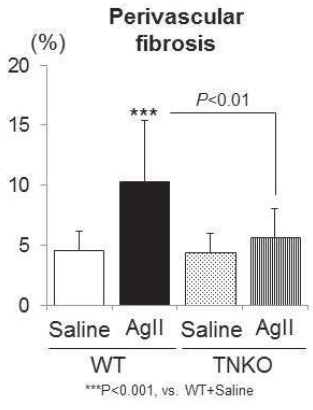
N. Shimojo [1], R. Hashizume [1], K. Kanayama [2], M. Hara [1], Y. Suzuki [1], T. Nishioka [1], T. Yoshida [1], K. Imanaka-Yoshida [1]. *[1] Mie University Graduate School of Medicine, Department of Pathology and Matrix Biology, Mie, JAPAN, [2] Mie University Graduate School of Medicine, Department of Pathologic Oncology, Mie, JAPAN*

Objective: Tenascin-C (TN-C) is an extracellular matrix glycoprotein, which is undetectable in the normal adult heart but expressed under various pathological conditions. We have previously reported about enhanced TN-C production and accumulation of macrophages in the perivascular region of mouse models with angiotensin II (AgII)-induced cardiac fibrosis. To clarify the molecular role of TN-C, we analyzed the effect of TN-C in a hypertensive heart by comparing wild-type (WT) and TN-C knock-out (TNKO) mice. Furthermore, to assess whether TN-C is involved in macrophage activation, we performed an in vitro study using macrophages isolated from the peritoneal cavity of WT mice.

Design and method: At 8 weeks of age, Balb/c WT and TNKO mice were subcutaneously implanted with an osmotic minipump which released AgII (560 ng/kg body weight/min) and euthanized 4 weeks later (WT/AgII and TNKO/AgII); they were subsequently analyzed using histological and molecular biological approaches.

Results: We found that AgII treatment (WT/AgII and TNKO/AgII) increased blood pressure, heart weight/body weight ratio, atrial and brain natriuretic peptide expression level and cardiomyocyte size, compared with non-AgII treated control groups (WT/Saline and TNKO/Saline). However, no significant differences were detected between WT/AgII and TNKO/AgII mice. In TNKO/AgII mice, interstitial collagen fibers (5.68±2.36 vs. WT/AgII: 10.29±5.09%, $p<0.01$) and accumulation of mac-3 positive macrophages (28±11.45 vs. WT/AgII: 50±15.13 cells/section, $p<0.01$) were reduced significantly compared with those of WT/AgII in the perivascular region. Additionally, mRNA expressions of interleukin (IL)-6 (0.72±0.36 vs. WT/AgII: 1.85±0.39 fold, $p<0.01$) and monocyte chemoattractant protein (MCP)-1 (2.10±0.49 vs. WT/AgII: 3.20±0.53 fold, $p<0.05$) were decreased. Using an in vitro migration assay, we found that TN-C accelerated macrophage migration in the presence of MCP-1. Western blotting and Immunofluorescence staining indicated that TN-C activated NF-kappaB rapidly. Quantitative PCR analysis demonstrated that TN-C up-regulated IL-6 (39.90±18.10 fold, $p<0.01$) and MCP-1 (3.14±0.11 fold, $p<0.001$) mRNA in an NF-κB dependent manner. Interestingly, NF-κB activation and IL-6 mRNA expression were suppressed by integrin αVβ3 antagonist P11.

Conclusions: TN-C accelerates IL-6 production by activating integrin αVβ3/NF-κB on macrophages and aggravating perivascular inflammation, thereby accelerating fibrosis in a hypertensive heart.



PP.05.11 THE EFFECTS OF IRON RESTRICTION ON HYPERTENSION AND RENAL INJURY IN ALDOSTERONE/SALT-INDUCED HYPERTENSIVE MICE

H. Sawada, Y. Naito, M. Oboshi, T. Iwasaku, Y. Okuhara, D. Morisawa, A. Eguchi, K. Nishimura, S. Hirotani, T. Masuyama. *Hyogo College of Medicine, Department of Internal Medicine, Cardiovascular Division, Nishinomiya, JAPAN*

Objective: Excess iron is associated with the pathogenesis of several cardiovascular diseases. We have previously shown that dietary iron restriction (IR) prevents hypertensive cardiovascular remodeling in Dahl salt-sensitive hypertensive rats. However, it has not been investigated the effects of IR on hypertensive renal injury. The aim of this study is to investigate the effects of dietary IR on the development of hypertension and renal injury in aldosterone/salt-induced hypertensive mice.

Design and method: Ten-week-old male C57BL/6J mice (25-27g) were uninephrectomized and infused aldosterone (0.15μg/hr) with osmotic minipumps for 4 weeks. Aldosterone-infused mice were divided into 2 groups: one fed a high-salt diet (Aldo, n=8) and the other fed a high-salt with iron-restricted diet (Aldo-IR, n=8). Saline-infused mice given a normal diet were served as controls (Control, n=6).

Results: Aldo mice showed progressive increase in systolic blood pressure compared with Control mice (114±8 vs 146±4mmHg, $p<0.05$), while it was suppressed in Aldo-IR mice (146±4 vs 119±5mmHg, $p<0.05$). Urinary albumin/creatinine ratio was increased in Aldo mice compared with Control mice (35.7±7.1 vs 361.5±67.7μg/mg, $p<0.05$), which was attenuated by IR (361.5±67.7 vs 162.9±34.6μg/mg, $p<0.05$). Moreover, urinary 8-Hydroxydeoxyguanosine/creatinine ratio was markedly increased in Aldo mice compared with Control mice (9.4±0.6 vs 20.8±2.1μg/mg, $p<0.05$), whereas its ratio was decreased by IR (20.8±2.1 vs 13.7±1.1μg/mg, $p<0.05$). In addition, renal histology revealed that Aldo mice exhibited glomerulosclerosis and tubulointerstitial fibrosis. In contrast, these histological changes were attenuated in Aldo-IR mice compared with Aldo mice. Interestingly, Western blot analysis showed that the renal expression of transferrin receptor 1 (TfR1), which is iron transport protein, was up-regulated in Aldo mice compared with Control mice. Immunohistochemistry further showed that TfR1 was expressed in the renal tubules in Aldo mice.

Conclusions: Dietary iron restriction attenuated the development of hypertension and renal injury in aldosterone/salt-induced hypertensive mice. Dysregulation of renal iron transport may be involved in the mechanism of salt-sensitive hypertension.

PP.05.12 MARKERS OF DYSFUNCTION OF AORTA AT EXPERIMENTAL ARTERIAL HYPERTENSION

V. Nevzorova [1], N. Zacharchuk [1], E. Gonchar [1], A. Sakovskaya [1], T. Brodskaya [1], I. Agafonova [2]. *[1] Pacific State Medical University, Vladivostok, RUSSIA, [2] Pacific Institute Bioorganic Chemistry Far-Eastern, Department Russian Academy of Science, Vladivostok, RUSSIA*

Objective: To evaluate vasomotor activity of the aorta in experimental modeling of hypertension.

Design and method: Hypertension in rats simulated by blocker of NO- synthase -N- nitro-L- arginine (received per os 50 mg / kg / day during 8 weeks) causes a persistent increase in blood pressure, reaching values of hypertension III degree (table 1) .We investigated vasomotor function of rats aorta by changing of diameter of it via assessment of magnetic resonance imaging before and after administration of vasodilators (acetylcholine and nitroglycerin) and vasoconstrictor (N- monomethyl -L-arginine and norepinephrine). The quantity of vasomotor responses calculated according to the formula : vasomotor response = (d2 - d1 / d1) × 100 %, where d1 - original diameter of aorta, d2 - diameter of aorta after the test . Variation of diameter of aorta less than 10 % after test considered as pathological vasomotor reaction.

Results: Contravention of vasomotor function of aorta estimated in experimental hypertension. Injection of acetylcholine and nitroglycerin caused a small increasing of diameter of aorta, which indicates a lack of vasodilation (table 1). Injection of N- monomethyl -L-arginine induced unequal pathological vasodilatation of aorta and the same time Injection of norepinephrine didn't cause expected vasoconstriction of aorta (table 1).

Index	The control group	The experimental group
Systolic blood pressure	123,9±9,9	182,13±13,4*
Diastolic blood pressure	76,8±5,6	111,9±4,4*
EDVD, % (Injection of acetylcholine)	+ 11,5 ±1,25	+5,59±0,58*
EUDVD % (Injection of nitroglycerin)	+ 17,8±0,98	+2,85±0,34*
EDVC, % (Injection of N- monomethyl -L-arginine)	- 7,9 ±0,14	+0,95±0,09*
EUDVC, % (Injection of norepinephrine)	- 5,4 ±0,12	-6,23±0,22*

Note: EDVD – endoteliodependent vasodilation; EUDVD – endotelioindependent vasodilation; EDVC - endoteliodependent vasoconstriction; EUDVC endotelioindependent vasoconstriction; * - the significant differences between the control and experimental groups, p <0.05

Conclusions: Simulation by hypertension induced by L-NAME NO deficiency causes a persistent increasing of blood pressure in rat and, consequently, impaired endothelial vasomotor function of aorta connected with insufficiency of vasodilator part of regulation and missing equal reaction to vasoconstriction.

PP.05.13 MARKERS OF ENDOTHELIAL DYSFUNCTION OF CEREBRAL ARTERIES IN EXPERIMENTAL ARTERIAL HYPERTENSION

V. Nevzorova [1], N. Zaharchuk [1], A. Sakovskaya [1], E. Gonchar [1], T. Brodskaya [1], I. Agafonova [2]. *[1] Pacific State Medical University, Vladivostok, RUSSIA, [2] Pacific Institute Bioorganic Chemistry Far, Eastern Department Russian Academy of Science, Vladivostok, RUSSIA*

Objective: To evaluate endothelial vasomotor activity of the cerebral vessels in experimental modeling of hypertension.

Design and method: Hypertension in rats simulated by blocker of NO- synthase -N- nitro-L- arginine (received per os 50 mg / kg / day during 8 weeks) causes a persistent increase in blood pressure, reaching values of hypertension III degree (table 1) .We investigated vasomotor function of cerebral vessels in rats by changing of diameter of the middle cerebral artery via assessment of magnetic resonance imaging before and after administration of vasodilators (acetylcholine and nitroglycerin) and vasoconstrictor (N- monomethyl -L-arginine and norepinephrine). The quantity of vasomotor responses calculated according to the formula: vasomotor response = (d2 - d1 / d1) × 100 %, where d1 - original diameter of artery, d2 - diameter of the artery after the test. Variation of diameter of middle cerebral artery less than 10 % after test considered as pathological vasomotor reaction.

Results: Contravention of vasomotor function of cerebral vessels estimated in experimental hypertension. Injection of acetylcholine and nitroglycerin caused a small increasing of diameter of middle cerebral artery, which indicates a lack of vasodilation (table 1). Injection of N- monomethyl -L-arginine and norepinephrine induced unequal vasoconstriction of cerebral vessels (table 1).

Index	The control group	The experimental group
Systolic blood pressure	123,9±9,9	182,13±13,4*
Diastolic blood pressure	76,8±5,6	111,9±4,4*
EDVD, % (Injection of acetylcholine)	+ 11,89±0,98	+ 6,87±0,88*
EUDVD % (Injection of nitroglycerin)	+ 17,84±1,25	+ 7,93±0,53*
EDVC, % (Injection of N- monomethyl -L-arginine)	- 7,9 ±0,14	- 1,58±0,15*
EUDVC, % (Injection of norepinephrine)	- 5,4 ±0,12	- 3,17±0,12*

Conclusions: Simulation by hypertension induced by L-NAME NO deficiency causes a persistent increasing in blood pressure in rat and, consequently , impaired endothelial vasomotor function of cerebral vessels connected with insufficiency of vasodilator part of regulation.

PP.05.14 ALBUMINURIA BREAKTHROUGH IS ASSOCIATED WITH AN ENHANCEMENT OF OXIDATIVE STRESS IN HYPERTENSIVE PATIENTS UNDER CHRONIC RENIN-ANGIOTENSIN SYSTEM SUPPRESSION

G. Ruiz-Hurtado [1], L. Condezo-Hoyos [2], H. Pulido-Olmo [3], I. Aranguez [4], M. González [2], S. Arribas [2], C. Cerezo [1], J. Segura [1], M. Praga [5], M. Fernández-Alfonso [3], L.M. Ruilope [1]. *[1] Unidad de Hipertensión, Instituto de Investigación imas12, Hospital Universitario 12 de Octubre, Madrid, SPAIN, [2] Departamento de Fisiología, Facultad de Medicina, Universidad Autónoma de Madrid, Madrid, SPAIN, [3] Instituto Pluridisciplinar and Facultad de Farmacia, Universidad Complutense de Madrid, Madrid, SPAIN, [4] Departamento de Bioquímica, Facultad de Farmacia, Universidad Complutense de Madrid, Madrid, SPAIN, [5] Division of Nephrology, Instituto de Investigación Imas 12, Hospital Universitario 12 de Octubre, Universidad Complutense, Madrid, SPAIN*

Objective: We investigated whether albuminuria escape observed in hypertensive patients under chronic renin-angiotensin system (RAS) suppression could be related to an increase in oxidative stress at systemic level.

Design and method: We studied normoalbuminuric (n=21) and de-novo albuminuric (n=20) patients in stage 2 chronic kidney disease (CKD) arriving to our hospital-based Hypertension Unit. The relationship between albuminuria breakthrough and circulating biomarkers for both oxidative damage, i.e. carbonyl and malondialdehyde (MDA), as well as anti-oxidant defense, i.e. reduced glutathione, thiol groups, uric acid, bilirubin, or catalase and superoxide scavenging activity, was assessed.

Results: We found that only patients with albuminuria escape showed an important increase in carbonyls ($P<0.001$) and MDA ($P<0.05$) compared to normoalbuminuric patients. This increase in oxidative damage was also accompanied by a rise in catalase activity ($P<0.05$) and low-molecular-weight antioxidants only when they were measured as total antioxidant capacity ($P<0.01$). In order to establish the specific oxidative status of each group new indexes of oxidative damage and antioxidant defense were calculated with all these markers following a mathematical and statistical approach. Although both prooxidant and antioxidant indexes were significantly increased in de-novo albuminuric patients, only the oxidative damage index positively correlated with the increase of albumin/creatinin ratio ($P=0.0024$).

Conclusions: We conclude that new-onset albuminuria may amplify oxidative damage in patients in early stage of CKD. These results indicate that chronic RAS protection must be directed to avoid development of new-onset albuminuria and oxidative damage.

PP.05.15 INVESTIGATION OF AGE-RELATED CHANGES ON LEFT VENTRICULAR MYOCARDIAL SYSTOLIC DEFORMATION IN SPONTANEOUSLY HYPERTENSIVE RATS

Q. Ruan.
The first affiliated Hospital of Fujian Medical University, Fuzhou, CHINA

Objective: An accurate assessment of age-related changes on left ventricular(LV) contractile properties together with LV remodling in spontaneously hypertensive rats(SHR) could provide a scientific basis for selecting appropriate time point in related research in an animal models. This study aimed to investigate myocardial multi-dimensional systolic deformation at 12 to 82 weeks of SHR using 2-dimensional strain echocardiography (2DSE) and to explore the age-related changes on left ventricular contractile properties.

Design and method: Sixty 12-week old male SHR were divided into six groups and studied at 12,16,28,45,66and 82 weeks of age respectively. Echocardiographic measurements were acquired including LV diameter, wall thickness, left atrial size and LVEF; 2DSE measurements included endsystolic LV longitudinal strain (SL) , radial strain (SR),circumferential strain (SC). Invasive LVEDP and LV±dp/dtmax were detected within 2 hours after echocardiagraphic studies.

Results: LV wall thickness increased after 28 weeks,and to the peak at 66 weeks($p<0.05$); LV diameter, LVMI and left atrial size were significantly increased from 16 to 82 weeks; Decreased LVEF was only found at 82 weeks. Myocardial strain(SC, SR, SL) began to increase from 16 weeks, and to the peak at 28 weeks ($p<0.05$), no significant difference among the groups of 28, 46 and 66 weeks($p>0.05$), lowered only at 82 weeks ($p<0.05$). LV±dp/dtmax increased from 12 weeks to 16 and 28 weeks and then decreased form 28-82weeks(all $p<0.05$). Myocardial SC,SR,SL were found correlated with LVMI positively($r=0.61\sim0.71$, all $p<0.05$) when LVMI<17.5g/m2 and negatively($r= 0.50\sim0.75$, all $p<0.05$) when LVMI>17.5g/m2.

Conclusions: Age-related changes of LV myocardial systolic deformation occurred in SHR, with increases before 28 weeks and attenuation after that, suggesting a developmental as well as compensted myocardial contractile function when LVMI increase slightly in the early stage and a hypertensive pathologic decreases in the later period.

PP.05.16 EFFECT OF SUB ACUTE HYDRATATION VARIATIONS ON CENTRAL AND BRACHIAL PULSE PRESSURE

H. Ribeiro [1], M. Briet [1], A. Blanchard [1], E. Curis [1], X. Jeunemaitre [1,2], M. Azizi [1]. *[1] Centre de Investigation Clinique 9201, Hôpital Européen Georges Pompidou, AP-HP, Université Paris Descartes, Paris, FRANCE, [2] Service de Génétique, Hôpital Européen Georges Pompidou, AP-HP, Université Paris-Descartes, Paris, FRANCE*

Objective: We aimed to evaluate the effect of extracellular volume changes induced by dietetic and pharmacological interventions on central and brachial pulse pressure.

Design and method: 74 healthy male subjects, age (median [IQR]) 23,9 [5,7] years, non-smokers, were assigned to a low sodium/high potassium diet during seven days, followed by a high sodium/low potassium diet for 14 days, the last seven with concomitant administration of amiloride. Brachial blood pressure was measured using a validated electronic device (OMRON M6, Omron Co., Kyoto, Japan) and common carotid artery pressure waveforms were recorded non-invasively by aplanation tonometry (SphymoCor®, Atcor Medical, Sydney, Australia). Measurements were taken after 10 min of rest, at baseline, at 7th, 15th and 21st days. At baseline, 6th, 14th and 20th days patients had a 24h ambulatory blood pressure measurement, using SpaceLabs 90207 monitors.

Results: Changes in diet sodium content led to significant changes in weight, sodium urinary excretion, plasma aldosterone concentrations and renin activity, reflecting extracellular volume variation. Brachial pulse pressure significantly decreased during the dehydration period, increased during the hyperhydration period and came back to normal at day 21 whereas central pulse pressure remained stable during the three periods. In a mixed model analysis, age and visits at day 7 and 21 were independent determinants of changes in brachial pulse pressure.

Conclusions: Short time in increase in extracellular volume in associated with a decrease in peripheral pulse pressure but not central pulse pressure.

PP.05.17 THE IMPACT OF MASKED AND WHITE COAT HYPERTENSION ON APELIN AND RELAXIN PLASMA LEVELS

K. Zerva [1], M. Karali [1], D. Papadopoulos [1], D. Perrea [3], E. Sanidas [1], T. Makris [2] *[1] ESH Excellent Center of Hypertension, Laiko University Hospital, Athens, GREECE, [2] ESH Excellent Center of Hypertension, Elena Venizelou Maternity Hospital, Athens, GREECE, [3] Laboratory of Experimental Surgery, Medical School, Athens, GREECE*

Objective: Recent evidence demonstrate that masked hypertension (MH) is a significant predictor of cardiovascular disease, while white-coat hypertension (WCH), a common phenomenon is associated with impaired endothelial function, increased cardiovascular risk and is considered as a prognostic marker for the future development of established hypertension. On the other hand hypoapelinemia and hyporelaxinemia may contribute to vascular damage accelerating atherogenesis.
Aim of our study was to examine apelin and relaxin plasma levels in patients with MH and compare the findings to those of patients with WCH matched for age, sex, body mass index and the rest of risk factors.

Design and method: Out off one hundred-thirty (60 M, 70 F) healthy subjects mean age 45±12 yrs underwent 24 hour ambulatory blood pressure monitoring (ABPM). According to the BP recordings 24 individuals (8M, 16 F) had MH (daytime systolic blood pressure >= 135 mmHg or daytime diastolic blood pressure >= 85 mmHg - group A) and 32 healthy subjects (20M, 12F,) had WCH Apelin and relaxin plasma levels were determined in both groups (ELISA method).

Results: Our findings and the comparisons between the two groups are shown in the table below:

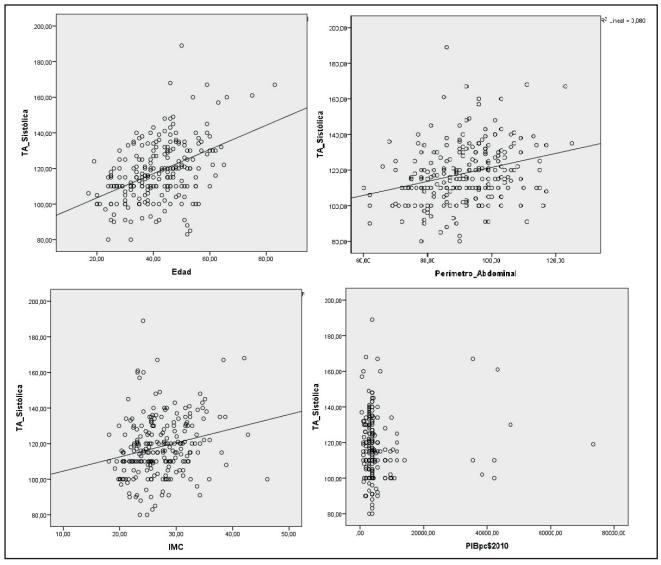
	Group A (n=24)	Group B (n=32)	p
Apelin (pg/ml)	200±111	305±127	<0.01
Relaxin (pg/ml)	35,2±6,7	46.8±23.6	<0.01

Conclusions: Our finding suggest that subjects with we have significantly lower apelin and relaxin plasma levels compared to subjects with VCH. This observation may have prognostic significance for future cardiovascular events in subjects with masked hypertension and needs further investigation.

PP.05.18 HYPERTENSION AND IMMIGRANTS

L. Noblia, K. Morales, B. Carrion, R. Requena, A. Marcos, G. Peralta, P. Molina
Centro de Salud Casco Antiguo, Cartagena, SPAIN

Objective: Hypertension correlates with other variables such as age, body mass index and per capita income in the country of origin.



Design and method: We conducted a descriptive observational study of a population sample of 234 patients obtained by simple random sampling from a population of 5 quotas urban health center in the period between January 15 and June 30, 2012, with a range of 95% confidence limit and a minor error at 0.05.

Results: In the statistical analysis the following results were obtained using Pearson correlation of different variables: SBP (systolic blood pressure) with BMI (body mass index) of 0.227 (p <0.01), 0.446 TAS with age (p <0.01) and TAS with PBIpc (gross domestic product per capita of the country) being -0.50 p 0.234 for this case. To DBP (diastolic blood pressure) the following results, TAD and 0.219 BMI (p <0.01) and age TAD 0.445 (P <00.1) and DBP were obtained with 0.28 PBIpc being 0.666 wt.

Conclusions: Both systolic blood pressure and diastolic blood pressure have a positive and significant correlation with increasing age and BMI as other studies have already demonstrated.
Moreover, the per capita income in the country of origin appears to be associated with increased odds tensions.

PP.05.19 SOLUBLE ADENYLYL CYCLASE IN VASCULAR ENDOTHELIUM: GENE EXPRESSION CONTROL OF ENAC-ALPHA, NA+/K+-ATPASE-ALPHA/-BETA AND THE MINERALOCORTICOID RECEPTOR

J. Nedele 1, B. Schmitz [1,2], K. Guske [1], M. Maase [3], M. Lenders [1], M. Schelleckes [1], K. Kusche-Vihrog [3], S.M. Brand [2], E. Brand [1]. *[1] University Hospital Münster, Internal Medicine D, Nephrology, Hypertension and Rheumatology, Münster, GERMANY, [2] University Hospital Münster, Institute of Sports Medicine, Molecular Genetics of Cardiovascular Disease, Münster, GERMANY, [3] University of Münster, Institute of Physiology II, Münster, GERMANY*

Objective: Components of the Renin-Angiotensin-Aldosterone-System (RAAS) are expressed and regulated in vascular endothelial cells. In particular, the epithelial Na+-channel (ENaC), the mineralocorticoid receptor (MR), and the Na+/K+-ATPase have been reported to regulate endothelial stiffness in response to serum Na+. In the current work, we determined the effect of sAC inhibition on endothelial stiffness. Furthermore, we analyzed sAC-dependent CRE-mediated transcriptional activation and the effects of sAC inhibition on ENaC-α, Na+/K+-ATPase-α/-β and MR expression on mRNA and protein levels.

Design and method: We determined the contribution of sAC to transcriptional activation in vascular endothelial cells (EC) and kidney collecting duct cells. Inhibition of sAC by the specific inhibitor KH7 reduced CRE-mediated promoter activity via reduction of CREB phosphorylation. KH7 and anti-sAC siRNA decreased mRNA and protein levels of ENaC-α and Na+/K+-ATPase-α. In Chromatin Immunoprecipitation (ChIP) experiments, sAC-dependent changes of CREB-p binding at ENaC and Na+/K+-ATPase-α promoter regions were analyzed. Using atomic force microscopy (AFM), a nano-technique that measures stiffness and deformability of living cells, we detected endothelial cell softening in mice aortae after sAC inhibition.

Results: Pharmacological inhibition of sAC by KH7 significantly decreased transcriptional activity of the CRE control vector ($p<0.05$). In addition, phosphorylated CREB was significantly reduced after KH7 treatment ($p<0.05$), whereas unphosphorylated CREB remained unaffected. Inhibition of sAC by KH7 and siRNA reduced expression of ENaC-α, Na+/K+-ATPase-α1/β1 and sAC (all p values <=0.011). Additionally, sAC inhibition by siRNA decreased ENaC-α and Na+/K+-ATPase-α protein levels (all p values <=0.05). ChIP experiments in ECs revealed binding of CREB-p to ENaC-α and Na+/K+-ATPase-α promoters under basic conditions which was prevented by sAC inhibition. AFM measurements revealed that KH7-treated mouse aorta ECs were significantly softer than untreated cells and aldosterone-induced stiffening of mouse aorta ECs was prevented by sAC inhibition (all p-values<0.05).

Conclusions: Selective sAC inhibition prevents aldosterone-induced endothelial stiffening. The underlying mechanism involves gene expression regulation of ENaC-α and Na+/K+-ATPase-α1 and -β1. Additional studies are warranted to investigate the protective action of sAC inhibitors in humans for potential clinical use.

PP.05.20 EFFECT OF IRON RESTRICTION ON MONOCROTALINE-INDUCED PULMONARY VASCULAR REMODELING IN RATS

Y. Naito [1], M. Hosokawa [1], H. Sawada [1], T. Iwasaku [1], Y. Okuhara [1], D. Morisawa [1], A. Eguchi [1], S. Hirotani [1], T. Tsujino [2], T. Masuyama [1]. *[1] Cardiovascular Division, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, JAPAN, [2] Department of Pharmacy, Hyogo University of Health Sciences, Kobe, JAPAN*

Objective: Pulmonary hypertension (PH) is characterized by pulmonary vascular remodeling leading to right ventricular (RV) failure. Recently, iron deficiency is reported to be prevalent in patients with PH. However, the mechanism by which iron deficiency occurs in patients with PH remains unknown. Here, we investigate the effects of dietary iron restriction on the development of monocrotaline-induced pulmonary vascular remodeling and the involved mechanisms.

Design and method: Male Sprague-Dawley rats were subcutaneously injected with monocrotaline (60 mg/kg). Afterwards, monocrotaline-injected rats were randomly divided into two groups and were given a normal diet (n=6) or an iron-restricted diet (n=6) for 4 weeks. Saline-injected rats given a normal diet were served as controls (n=6).

Results: Monocrotaline-injected rats showed pulmonary vascular remodeling, increased RV pressure, RV hypertrophy, and decreased RV ejection fraction, followed by RV failure after 4 weeks. In contrast, iron restriction attenuated the development of pulmonary vascular remodeling and RV failure. Of interest, expression of cellular iron transport protein, transferrin receptor 1 was increased in the pulmonary remodeled artery and the failing right ventricle of monocrotaline-injected rats, as compared with the controls. Moreover, a key regulator of iron homeostasis, hepcidin gene expression was increased in the failing right ventricle of monocrotaline-injected rats.

Conclusions: Iron restriction attenuated the development of monocrotaline-induced pulmonary vascular remodeling and RV failure. Cellular iron transport might be involved in the pathophysiology of PH and PH induced RV failure.

PP.05.21 PRENATAL CORTISOL EXPOSURE AFFECTS THE BLOOD PRESSURE IN LATER LIFE

F. Mori [1], T. Shimosawa [2], R. Jimbo [3], D. Hirohama [2], D. Watanabe [1], T. Ando [1], S. Morimoto [1], T. Fujita [4], A. Ichihara [1]. *[1] Tokyo Women's Medical University, Hypertension and Endocrinology, Tokyo, JAPAN, [2] University of Tokyo, Faculty of Medicine, Endocrinology and Nephrology, Tokyo, JAPAN, [3] Tokyo Hitachi Hospital, Tokyo, JAPAN, [4] University of Tokyo, Division of Clinical Epigenetics, Research Center for Advanced Science and Technology, Tokyo, JAPAN*

Objective: It is known that the prenatal stress is a risk factor for the metabolic disease and emotional disorders. This change is permanent and induced by epigenomic changes. The aim of this study is to investigate whether fetal stress would affect the blood pressure control in the central nervous system.

Design and method: We injected dexamethasone (200mg/kg/d, Dex group) or saline (Control group) intraperitoneally to pregnant Sprague-Dawley rat (from F15 to F20).

Results: The body weight of Dex group (14.8±0.5 g) at the 7 post-natal day (P7) is lower than Control group (15.2±0.4 g , $p<0.05$), whereas it is much higher at the 12 weeks (Dex:552.5±3.9 g, C: 393.8±9.4, $p< 0.001$)
To investigate whether the blood pressure is elevated in the Dex group, we measured blood pressure using telemetry system or direct measurement via carotid artery with normal, 8% salt (HS), and 0.05% salt (LS) diet loading at the 12 weeks. Blood pressure is elevated after salt loading in Dex group (Dex_HS 159.5±3.4mmHg, Dex_NS group:142.8±1.9mmHg, $p<0.05$). Next we evaluated urine catecholamine, which was suppressed by salt loading, and its degree was weaker in the Dex group than Control group. Importantly this phenomenon is one of the causes of salt sensitivity.
To examine whether DNA methylation status is affected by dex, we evaluated the mRNA expressions of methylation enzyme (DNMT1, DNMT3a, 3b) in hypothalamus and DNMT3a and 3b were downregulated in the Dex group. Further, we injected demethylating agent, 5-Aza-2'-deoxycitydine intraventricularly to the male SD rats, measured the blood pressure loading HS and LS by telemetry system. Importantly DNA demethylation in the CNS induced salt sensitive hypertention.
We hypothesized that renin-angiotensin system and ROS would be affected by metylation enzyme. However, mRNA expressions of the AT1a, AT1b, NR3C1 and NR3C2 were not different between Control and Dex group, nor NOX2 or NOX4, NADPH oxidase component, though the mRNA change by salt loading were different between groups.

Conclusions: The DNA methylation state in the hypothalamus changed with the stress exposure in an embryo and a possibility that it had contributed to salt susceptibility high blood pressure was suggested.

PP.05.22 OSTEOGENIC FACTORS, OSTEOPROTEGERIN AND FETUIN-A ARE NEW PLAYERS IN VASCULAR DAMAGE ASSOCIATED WITH HYPERTENSION

A. Montezano, K. Neves, R. Lopes, D. Graham, R.M. Touyz. *Institute of Cardiovascular and Medical Sciences, BHF GCRC, Glasgow, UNITED KINGDOM*

Objective: Osteoprotegerin (OPG) and fetuin-A (FetA) are inhibitors of vascular calcification, while at the same time they are associated with cardiovascular risk in cardiovascular diseases. The direct vascular effects of OPG and FetA remain unclear. Here we postulated that in hypertension increased levels of osteogenic factors may promote vascular injury.

Design and method: Aortic tissue and vascular smooth muscle cells (VSMCs) from WKY and SHRSP (16-18 weeks) rats were studied. VSMCs were stimulated with recombinant OPG and FetA (25 – 500ng) from 1 to 30 minutes. Vascular calcification was assessed by Von Kossa staining. OPG, TRAIL, FetA expression, as well as JNK, p38 and ERK1/2 activation were assessed by immmunoblotting. ROS generation was studied by chemiluminescence.

Results: Aorta from SHRSP, but not WKY, exhibited positive Von Kossa staining. Levels of osterix (86%), OPG (20%), and TRAIL (28%) were increased in VSMCs from SHRSP rats. OPG stimulation of VSMCs from WKY and SHRSP induced ROS generation (100ng/5min: WKY – 40% increase; SHRSP – 75% increase, $p<0.05$ vs vehicle); an effect blocked by c-Src inhibitor PP2 and Nox4/1 inihibitor (GKT137831) but not Nox1 inhibitor (ML171). FetA stimulation also induced ROS generation in VSMCs from WKY and SHRSP rats (50ng/5min: WKY – 50% increase; SHRSP – 50% increase, $p<0.05$ vs vehicle), which was blocked by PP2 and Nox1 inhibitors (GKT137831 and ML171). JNK (75% WKY; SHRSP 200%), p38 (110% WKY; 100% SHRSP) and ERK1/2 (100% WKY; 100% SHRSP) were activated by OPG 50ng ($p<0.05$). FetA only increased ERK1/2 (50%) in VSMCs from WKY and; in SHRSP, increased ERK1/2 and p38 by 75% and 50% respectively ($p<0.05$). In addition, OPG (75%) and FetA (40%) levels were increased in LinA3 mice, a mouse model which has chronically elevated Ang II levels. Ang II (10-7mol/L) stimulation of VSMCs from WKY rats induced an increase of OPG levels.

Conclusions: These data suggest that in hypertension, OPG and FetA may influence vascular damage through redox-sensitive signalling. Identification of vascular calcification-derived osteogenic factors as modulators of VSMCs biology provides new insights into molecular mechanisms of vascular injury in hypertension.

PP.05.23 DIFFERENCES IN NITRIC OXIDE SYNTHASE ACTIVITY DOES NOT AFFECT BLOOD PRESSURE IN RATS WITH METABOLIC SYNDROME

Z. Matuskova, S. Vrankova, J. Klimentova, A. Barta, M. Kovacsova, O. Pechanova *Institute of Normal and Pathological Physiology SAS, Bratislava, SLOVAK REPUBLIC*

Objective: The aim of this study was to determine nitric oxide synthase activity (NOS) in the peripheral organs and in the parts of central nervous system of young and adult rats with metabolic syndrome (MS) represented by obese, spontaneously hypertensive rats [SHR/ND mcr-cp (cp/cp)].

Design and method: Animals were divided into four groups: male young 8-9-week-old and adult 14-15 week-old MS rats and control, normotensive, age-matched Wistar Kyoto rats (WKY). Blood pressure was measured by tail-cuff plethysmography. NOS activity was determined by measuring the formation of L-[3H] citrulline from L-[3H] arginine in the peripheral organs (aorta, heart, kidney) and brain parts (cerebellum, brain cortex and brain steam).

Results: Blood pressure of young WKY rats was 120±4 mmHg and did not change within six weeks. Interestingly, NOS activity of adult WKY in the peripheral organs increased significantly in comparison with young WKY, while it was not changed in the brain parts investigated. On the other hand, NOS activity of adult MS rats decreased significantly in both peripheral organs and brain regions in comparison with young MS rats. This decrease, however, did not affect blood pressure of adult MS rats. There were no changes in NOS activity of young MS rats and age-matched WKY except of the aorta. NOS activity in this respective tissue was higher in young MS rats. Since both blood pressure and NOS activity of brain parts in young and adult WKY did not changed we hypothetised that nitric oxide produced in the brain may be responsible predominantly for blood pressure maintenence in WKY. In MS rats, however, despite decreased NOS activity in the brain, blood pressure remained on the level of young animals.

Conclusions: In conclusion, our results indicate that other mechanisms than NO/cGMP pathway may be responsible for blood pressure maintenance in rats with metabolic syndrome.

PP.05.24 HETEROZYGOUS DISRUPTION OF ACTIVIN RECEPTOR-LIKE KINASE 1 IS ASSOCIATED WITH INCREASED ARTERIAL PRESSURE

J. Lopez-Novoa [1], M. Gonzalez-Nuñez [1], A. Sanchez-Riolobos [1], O. Castellano [2], M. Pericacho [1], I. Fuentes-Calvo [1], M. Sevilla [1], F. Perez-Barriocanal [1]. *[1] Department of Physiology and Pharmacology, University of Salamanca, Salamanca, SPAIN, [2] Institute of Neurosciences, University of Salamanca, Salamanca, SPAIN*

Objective: The Activin receptor-like kinase-1 (ALK-1) is a type I cell surface receptor for the TGF-β family of proteins. Hypertension, a predominant risk factor for stroke, coronary heart disease or chronic kidney disease, is related to the ALK-1 ligand TGF-β1 as increased TGF-β1 expression correlate with an elevation in arterial pressure (AP) and TGF-β expression and signalling is also up-regulated by the renin-angiotensin-aldosterone system. Thus the purpose of this study has been to assess the role of ALK-1 in regulating AP using a mice model of ALK-1 haploinsufficient (ALK-1+/-), as ALK-1 KO mice are not viable (Oh P et al. Proc Natl Acad Sci U S A. 2000;97:2626-31).

Design and method: AP and heart rate were measured by the tail cuff method and by radiotelemetry. Locomotor activity was also measured by telemetry. Transthoracic echocardiography was performed using a) cardiac ultrasound machine equipped with a 10-14-MHz transducer. Telemetric electrocardiogram (ECG) were performed using an implantable telemetry system.

Results: Systolic or diastolic AP measured either by tail-cuff or by telemetry showed higher values in ALK-1+/- than in ALK-1+/+ mice with no significant differences in heart rate. All functional and structural parameters, either directly measured by echocardiography or calculated, were similar in both groups of animals. Electrocardiographic analysis revealed no apparent abnormalities in control or ALK-1+/- mice. ALK-1+/- mice shows alterations in arterial pressure

circadian rhythm: the lower arterial pressures in ALK-1+/+ mice were observed during the light period (from 10 am to 8 pm) whereas ALK-1+/- mice maintain higher arterial pressure than ALK-1+/+ mice during most of the light period. ALK-1+/- mice show neither alterations in the nitric oxide -cGMP vasodilator system nor in the peripheral renin-angiotensin system. ALK-1+/- mice shows sympathetic nervous system overactivation characterized by and increased hypotensive response to the β-adrenergic antagonist atenolol and increased plasma levels of epinephrine and norepinephrine.

Conclusions: These data suggest that high AP shown by ALK-1+/- mice is explained mainly by the sympathetic overactivation shown by these animals, and that the ALK-1 receptor for TGF-β and BMPs is involved in the control of arterial pressure.

PP.05.25 RENOPROTECTIVE EFFECT OF VASOPRESSIN V2 RECEPTOR ANTAGONIST TOLVAPTAN IN DAHL RATS WITH END-STAGE HEART FAILURE

N. Kobayashi, S. Onoda, A. Nagase, Y. Ueno, T. Ishimitsu
Dokkyo Medical University, Tochigi, JAPAN

Objective: Tolvaptan is the highly selective and orally effective arginine vasopressin V2 receptor antagonists, and is potentially useful for treatment of heart failure (HF) patients. However, the renoprotective effect of long-term tolvaptan therapy and its underlying mechanisms remain unknown. We evaluate the effects of chronic treatment with tolvaptan on renal dysfunction, podocyte injury, inflammation, and oxidative stress, Rho-kinase, epithelial-mesenchymal transition (EMT), and extracelluar signal-regulated protein kinase (ERK1/2) pathway in the renal cortex of Dahl salt-sensitive hypertensive (DS) rats with end-stage severe HF.

Design and method: DS and Dahl salt-resistant rats were fed a high-salt diet at 6 weeks of age. DS rats were treated with vehicle and tolvaptan (0.05% concentration in diet) from the age of 11 to 18 weeks.

Results: Vehicle-treated DS rats developed proteinuria, renal dysfunction, glomerulosclerosis, and interstitial fibrosis, which were ameliorated by tolvaptan without changing blood pressure. Decreased expression of nephrin and podocin and increased desmin-positive area in failing rats were restored by tolvaptan. Upregulation of NAD(P)H oxidase p22phox, p47phox, and gp91phox, EMT marker such as transforming growth factor-β1, vimentin, and fibronectin expression, and Rho-kinase and ERK1/2 phosphorylation in DS rats was significantly suppressed by tolvaptan. Tolvaptan administration resulted in significant inhibition in tumor necrosis factor-α and monocyte chemoattractant protein-1 expression, and nuclear factor-κB phosphorylation.

Conclusions: We concluded that long-term tolvaptan therapy may improve renal dysfunction, glomerulosclerosis, podocyte injury, and inflammation associated with oxidative stress, EMT, ERK, and Rho-kinase pathway in failing heart of DS rats. Thus, tolvaptan may be a therapeutic strategy for end-stage severe HF.

PP.05.26 RENOPROTECTIVE MECHANISMS OF TELMISARTAN ON RENAL INJURY AND INFLAMMATION IN SHRSP.Z-LEPRFA/IZMDMCR RATS

N. Kobayashi, S. Onoda, A. Nagase, Y. Ueno, T. Ishimitsu
Dokkyo Medical University, Tochigi, JAPAN

Objective: SHRSP.Z-Leprfa/IzmDmcr (SHRSP fatty) rats create a new animal model of metabolic syndrome. However, the renoprotective effect of telmisartan therapy and its underlying mechanisms in SHRSP fatty rats remain unknown. We evaluate the effects of long-term telmisartan therapy on renal dysfunction, podocyte injury, inflammation, and transforming growth factor-β1 (TGF-β1)/Smad, epithelial-mesenchymal transition (EMT), mitogen-activated protein kinase (MAPK), Rho-kinase, and cell-cycle progression pathway in the renal cortex of SHRSP fatty rats.

Design and method: Seven-week-old male SHRSP fatty rats were treated with vehicle, telmisartan, and hydralazine for 8 weeks. Age-matched male Wistar-Kyoto/Izumo rats served as a control group.

Results: Vehicle-treated SHRSP fatty rats developed proteinuria and renal dysfunction, which in the telmisartan group was less than the vehicle and hydralazine group without changing blood pressure. Glomerulosclerosis and interstitial fibrosis were impaired in SHRSP fatty rats, and these renal damage in the telmisartan group was less than the vehicle and hydralazine group. Decreased expression of nephrin and podocin and increased desmin-positive area in SHRSP fatty rats were restored by telmisartan but not hydralazine. TGF-β1/Smad, EMT marker, MAPK, Rho-kinase, and cell-cycle progression pathways were upregulated in SHRSP fatty rats, and these increased proteins in the telmisartan group were less than the vehicle and hydralazine group. Telmisartan administration resulted in significant suppression in tumor necrosis factor-α expression and nuclear factor-κB phosphorylation.

Conclusions: Long-term telmisartan therapy may improve renal dysfunction, glomerulosclerosis, podocyte injury, and inflammation associated with EMT, TGF-β/Smad, MAPK, Rho-kinase pathway in SHRSP fatty rats. Thus, telmisartan may have significant therapeutic potential for metabolic syndrome.

PP.05.27 ACTIVATION OF NUCLEAR FACTOR-KAPPA B UPREGULATES ENOS IN CENTRAL NERVOUS SYSTEM

J. Klimentova, S. Vrankova, M. Kovacsova, A. Barta, Z. Matuskova, O. Pechanova
Institute of Normal and Pathological Physiology, SAS, Bratislava, SLOVAK REPUBLIC

Objective: Several studies have suggested the different nuclear factor NF-kappaB (NFkB) activation by nitric oxide (NO) in central nervous system (CNS) and cardiovascular system (CVS).

Design and method: The aim of our study was to determine NO and NF-kB generation at the level of CNS as well as CVS in normotensive and hypertensive rats. Male 9-week-old rats were divided into two groups: control Wistar Kyoto rats (WKY) and spontaneously hypertensive rats (SHR).
In our study was blood pressure measured by tail-cuff plethysmography. NO synthase activity was determined by measuring the formation of L-[3H] citrulline from L-[3H] arginine in the aorta, heart, cerebellum, brain cortex and brain stem. Protein expressions of endothelial NOS (eNOS), neuronal NOS (nNOS) and NF-kB were determined by Western blot analysis in the same tissues.

Results: Blood pressure was increased by 55% in SHR in comparison with age-matched control Wistar Kyoto rats. NOS activity was decreased significantly in the aorta and there was a decreased tendency in the heart. On the other hand, NOS activity in CNS was increased in the brain cortex and brain stem. While the expression of eNOS and NFkB was not changed in CVS, the expression of eNOS and NFkB was enhanced in CNS of SHR in comparison with normotensive WKY rats. No changes in nNOS expression were determined either in CVS or CNS.

Conclusions: This study indicates that increased NFkB expression as well as activation may upregulate eNOS leading to increased NOS activity and NO generation in the brain. Increased generation of NO seems to be however insufficient to counterbalance increasing blood pressure in SHR.

PP.05.28 COMPARISON OF METABOLIC PARAMETERS WITH HYPERTENSION. DETERMINATION AIDS

K. Kisters [1], M. Moser [2], K. Pichlkastner [2], H. Gell [2], A. Sadjag [3], S. Porta [2,3,4]
[1] Medical Clinic I, St. Anna Hospital, Herne, GERMANY, [2] Theresian Military Academy, Wiener Neustadt, AUSTRIA, [3] University Institute of Pathophysiology and Immunology, Graz, AUSTRIA, [4] University Institute of Applied Stress Research, Dillach, AUSTRIA

Objective: Comparison of simple metabolic parameters with blood pressure values are shown. Determination aids prognosis and avoids interpretation artefacts. The special role of lactate tests in the development of stress and hypertension is discussed.

Design and method: Out of 100 microliters of capillary blood of 25 officer trainees of the Theresian Military Academy of Wiener Neustadt in Austria, pH, pCO2 and lactate were determined by a NOVA Biomedical Phox-M device before and after a moderate run of 2400 m in standardized 11.5 minutes. Additionally, blood pressure values were measured under exercise.

Results: A significant negative correlation ($p < 0.05$) between systolic blood pressure values before the run and pCO2 after the run suggests that breathing frequency during moderate sports linearly depends upon basal systolc blood pressure values.
However, correlation between pH and pCO2, both after the run shows that exactly those participiants, who exclusively form the upper left end of the (systolic blood pressure values before/pCO2 after exercise) correlation, exhibit extremely low pH and pCO2 values along with very high lactate levels after the run, untypical for the majority of the group.
Removal of those outliners has a dovetailing effect: the significance of the (systolic blood pressure before/pCO2 after run) correlation fades away and the pH/pCO2 correlation after the run suddenly turns negatively significant ($p < 0.01$), typical for the reaction to a moderate workload.
This means that uncontrolled acceptance of even unobtrusively increased systolic blood pressur values in a group can easily lead to wrong conclusions and artefacts of interpretation of data, unless additional metabolic parameters like pCO2 or even lactate are introduced.
Disproportional lactate increases after the run are totally unpredictable by metabolic values before the run. Only their systolic blood pressure values are among

the highest values before the run. Accordingly, if any oversensitive reactions of participants to a moderate run should take place, the persons are to be found among those with the highest systolic blood pressure values before exercise.

Conclusions: The data presented here indicate that a sizeable increase of knowledge and safety of interpretation can thus be gained by a lactate test.

PP.05.29 ANTIHYPERLIPIDEMIC EFFECT OF MELOTHRIA MADERASPATANA LEAF EXTRACTS ON DOCA-SALT INDUCED HYPERTENSIVE RATS

A. Khalid, G. Chandramohan, M. Alsaif, C. Veeramani. *Department of Community Health Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, SAUDI ARABIA*

Objective: To investigate the antihyperlipidemic effect of crude ethanolic extract of Melothria maderaspatana (M. maderaspatana) leaf (CEEM) on deoxycorticosterone acetate (DOCA)-salt hypertensive rats.

Design and method: A midscapular incision was made on each rat and the left kidney was excised after ligation of the renal artery. The surgical wound was closed using an absorbable suture. After one week recovery period, hypertension was induced by subcutaneous injection of DOCA-salt solution, twice a week, and the rats received a 1% sodium chloride solution as drinking water throughout the experimental period. CEEM or nifedipine was administered orally once a day for 6 weeks.

Results: In DOCA-salt hypertensive rats, the level of plasma and tissues of total cholesterol (TC), triglycerides (TG), free fatty acids (FFA) and phospholipids (PL) significantly increased and administration of CEEM significantly reduced these parameters towards normality. Further, the levels of low density lipoprotein-cholesterol (LDL-C) and very low density lipoprotein-cholesterol (VLDL-C) significantly increased while high density lipoproteincholesterol (HDL-C) decreased in hypertensive rats and administration of CEEM brought these parameters to normality which proved their antihyperlipidemic action. Histopathology of liver, kidney and heart on DOCA-salt induced rats treated with CEEM showed reduced the damages towards normal histology.

Conclusions: These findings provided evidence that CEEM was found to be protecting the liver, kidney and heart against DOCA-salt administration and the protective effect could attribute to its antihyperlipidemic activities.

PP.05.30 FRACTAL ANALYSIS OF THE VARIATIONS IN ARTERIAL PRESSURE, HEART RATE, AND LOCOMOTOR ACTIVITY IN CONGENIC RATS

H. Kawamura [1], H. Mitsubayashi [2], N. Saito [3], K. Ikeda [4], K. Kawakami [5], T. Nabika [6]. *[1] MJG Cardiovascular Institute, Saitama-Shi, JAPAN, [2] Department of Medicine, Nippon Dental University School of Life Dentistry, Tokyo, JAPAN, [3] Department of Medicine, Kusatsu General Hospital, Kusatsu, JAPAN, [4] Department of Pharmacology, Mukogawa Women's University, Nishinomiya, JAPAN, [5] Department of Experimental Animals, Shimane University, Izumo, JAPAN, [6] Department of Functional Pathology, Shimane University School of Medicine, Izumo, JAPAN*

Objective: Congenic rats (SHRSPwch1.0) were derived from stroke-prone SHR/Izumo (SHRSP/Izm) and Wistar-Kyoto/Izumo (WKY/Izm) rats. We found that the SHRSPwch1.0 rats exhibited lower systolic arterial pressure (SAP) and heart rate (HR) values than the SHRSP/Izm rats. However, the SHRSPwch1.0 rats displayed markedly higher locomotor activity (ACT) than the SHRSP/Izm rats. The purpose of this study was to investigate the degree of long-range (>24 hours) fractal variability in the fluctuations in SAP, HR, and ACT seen in SHRSPwch1.0 rats.

Design and method: We used ten male mature SHRSPwch1.0 rats and ten male age-matched SHRSP/Izm rats as controls. The rats' SAP, HR, and ACT were monitored using radiotelemetry, and the variations in these parameters were subjected to the fast Fourier transformation for spectral analysis and detrended fluctuation analysis (DFA) to assess the parameters' long-range correlations.

Results: The SHRSPwch1.0 rats displayed lower SAP (194±7 vs. 229±7mmHg, P=0.0098) and HR (310±24 vs. 381±16 beats/min, P=0.0001) values than the SHRSP/Izm rats. The ACT counts of the SHRSPwch1.0 rats were higher than those of the SHRSP/Izm rats (62±47 vs. 26±26 counts/10sec, P<0.001). The frequencies of the variations in SAP, HR, and ACT all exhibited gradients of 1/f β in both rat strains. Spectral analysis revealed that the SAP and HR β values of the SHRSPwch1.0 rats were lower than those of the SHRSP/Izm rats (mean ± SD; SAP, 0.9715±0.0517 vs. 1.3091±0.0494; HR, 0.8105±0.0525 vs.1.0904±0.0587; both P<0.0002). However, the β value for ACT did not differ between the SHRSPwch1.0 and SHRSP/Izm rats. DFA analysis revealed that the α values for SAP, HR, and ACT ranged from 0.5-1.0 in both rat strains. However, the SHRSPwch1.0 rats demonstrated a markedly lower ACT α2 value than the SHRSP/Izm rats (0.2569±0.1354 vs. 0.8180±0.1116, P=0.0040).

Conclusions: Therefore, the variations in the SAP and HR of SHRSPwch1.0 rats are less fractal than those seen in SHRSP/Izm rats, and the ACT variations of SHRSPwch1.0 rats do not exhibit any long-range correlations.

PP.05.31 HYPOTENSIVE MECHANISM OF TELMISARTAN IN HIGH SALT-LOADING HUMAN RENIN AND ANGIOTENSINOGEN TRANSGENIC MICE

J. Iwanami [1], M. Mogi [1], T. Tsukuda [1], X. Wang [1], K. Ohshima [1,2], H. Nakaoka [1], T. Chisaka [1,3], H. Bai [1], L. Min [1], M. Horiuchi [1]. *[1] Ehime University, Department of Molecular Cardiovascular Biology and Pharmacology, Toon, JAPAN, [2] Ehime University, Department of Cardiology, Pulmonology, Hypertension and Nephrology, Toon, JAPAN, [3] Ehime University, Department of Pediatrics, Toon, JAPAN*

Objective: Hypertension is associated with an increase in sympathetic nerve activity. It is well known that excessive salt intake and/or activation of renin-angiotensin system (RAS) increases blood pressure partially via an increase in sympathetic nerve activity. Although high salt intake reduces circulating level of RAS, local tissue RAS is still activated. For example, it is reported that high salt intake increases angiotensin II in kidney and plasma. Here, we investigated the effect of salt loading on RAS activated mice and the preventive effect of telmisartan in these mice.

Design and method: Tsukuba hypertensive (TH: hRN/hANG-Tg) mice generated by cross-mating of human renin (hRN) and human angiotensinogen (hANG) transgenic mice were used in this study. Ten-week-old male TH mice were administrated control chow or 8% NaCl chow with or without 1 mg/kg/day telmisartan in drinking water for 8 weeks. Blood pressure was assessed by radio telemetry method. Urine samples were obtained before and 2, 4 and 8 weeks after salt-loading. Concentration of urine adrenalin and noradrenalin 8 weeks after treatment was measured by ELISA method.

Results: Body weight did not differ in all groups. Survival rate 8 weeks after treatment was decreased in salt-loading TH mice. This decrease was improved by treatment with telmisartan. Blood pressure in salt loading TH mice was significantly higher compared with control TH mice. Treatment with telmisartan in salt-loading TH mice significantly decreased blood pressure. Urinary sodium concentration was increased in salt-loading TH mice compared with control TH mice. Treatment with telmisartan in salt loading TH mice increased urinary sodium concentration compared with salt loading TH mice. Concentration of urinary adrenalin and noradrenalin were increased in salt-loading TH mice compared with control TH mice. This increase was attenuated by treatment with telmisartan.

Conclusions: These results suggested that salt-loading enhanced an increase in blood pressure and mortality in TH mice. Treatment with telmisartan increased survival rate through decrease in blood pressure, enhancement of natriuresis and attenuation of sympathicotonia.

PP.05.32 HYPOTENSIVE EFFECT OF CEREBELLAR ADRENOMEDULLIN

A. Israel, L. Figueira. *Laboratory Neuropeptides, School of Pharmacy, Universidad Central de Venezuela, Caracas, VENEZUELA*

Objective: Adrenomedullin (AM) is a 52-amino acid peptide which has important functions in cardiovascular regulation. In effect, peripherally administration of AM causes a marked decrease in blood pressure (BP). AM has two specific receptors formed by the calcitonin-receptor-like receptor (CLRL) and receptor activity-modifying protein (RAMP) 2 or 3. These are known as AM1 and AM2 receptors, respectively. In addition, AM has appreciable affinity for the calcitonin gene-1 related peptide receptor (CGRP1), composed of CRLR and RAMP1. In brain, AM and their receptors are located in localized areas, including cerebellum. Autoradiography and quantitative densitometry showed an increase in the AM density binding sites in the cerebellum during hypertension, suggesting a role of cerebellar adrenomedullinergic system in blood pressure control. Thus the objective was to assess the functional role of in vivo of cerebellar AM by in situ microinjection of AM in the cerebellar vermis.

Design and method: For this purpose, adult male spontaneously hypertensive rats (SHR) and control Wistar Kyoto (WKY) were used. The animals were anesthetized and cannulated in the cerebellar vermis. After recovery, animals were divided into three groups: AM (0.02 to 200 pmol/5µL), ANG II (200 pmol/5µL) and vehicle. Baseline blood pressure and after the treatments were determined by non invasive plethysmography. Cannulation was verified post-mortem with in situ microinjection of a dye solution.

Results: Our results demonstrate that microinjection of AM into the cerebellar vermis caused a profound dose dependent hypotensive response in SHR, but not in normotensive WKY rats (N=17, $p<0.05$). The hypotensive effect was specific, since in situ microinjection of vehicle or angiotensin II did not cause significant changes in BP.

Conclusions: Our findings suggest that cerebellar AM plays an important role in the regulation of BP and they constitute a novel mechanism of BP control which has not been described so far.

PP.05.33 LOSARTAN METABOLITE EXP3179 NORMALIZES CARDIAC HYPERTROPHY IN L-NAME INDUCED HYPERTENSION

J.L. Miguel-Carrasco [1], G. San José [1], M.U. Moreno [1], J. Beaumont [1], S. Ravassa [1], J. Díez [1], G. Zalba [2], A. Fortuño [1]. *[1] Division of Cardiovascular Sciences (CIMA), University of Navarra, Pamplona, SPAIN, [2] Department of Biochemistry and Genetics, University of Navarra, Pamplona, SPAIN*

Objective: Cardiac hypertrophy is an independent marker of mortality in hypertension. Losartan, an angiotensin II type 1 receptor antagonist, is able to attenuate cardiac hypertrophy associated to hypertension. Two active metabolites of the angiotensin type 1 receptor blocker losartan have been described previously, EXP3174 and EXP3179. Whereas EXP3174 is the main antihypertensive AT1 receptor-blocking metabolite, the role of EXP3179 is widely unknown. We investigated the effects of metabolites EXP3174 and EXP3179 on cardiac hypertrophy in L-NAME induced hypertension.

Design and method: The study was carried out in six groups of 10-week-old Wistar rats. Three groups were treated with vehicle, with EXP3179 (5 mg/kg/day), or with EXP3174 (5 mg/kg/day). The other 3 groups were exposed to L-NAME (30 mg/kg/day) and treated with vehicle, with EXP3179 (5 mg/kg/day), or with EXP3174 (5 mg/kg/day). During the period of treatment (10 weeks), systolic blood pressure and cardiac morphology and function was recorded by telemetry and echocardiography, respectively.

Results: The group of L-NAME rats developed hypertension and concentric cardiac hypertrophy, characterized by increased left ventricular mass index and relative wall thickness. The group of EXP3174-treated L-NAME rats was normotensive, although the EXP3174 did not prevent the concentric cardiac hypertrophy. The group of EXP3179-treated L-NAME rats developed also hypertension, although the EXP3179 was able to prevent the concentric cardiac hypertrophy. In addition, the higher expression of atrial natriuretic peptide in the heart of L-NAME rats was only prevented in the group of rats treated with EXP3179.

Conclusions: Thus, EXP3179 is able to prevent cardiac hypertrophy in the experimental hypertension associated with a chronic depletion of nitric oxide levels. It is proposed that the pleiotropism of the EXP3179 metabolite may confer to losartan specific capacities in the treatment of cardiac hypertrophy in arterial hypertension.

PP.05.34 PHYSICAL TRAINING ASSOCIATED WITH THE CHRONIC CHOLINERGIC STIMULATION IN HYPERTENSIVE RATS. EFFECTS ON ARTERIAL PRESSURE AND CARDIOVASCULAR AUTONOMIC CONTROL

K. Delgado Maida, J.H.D. Dutra Blanco, H.C. Dutra De Souza. *Biomechanics, Medicine and Rehabilitation, Program in Rehabilitation and Functional Performance, FMRP/USP, Ribeirão Preto, BRAZIL*

Objective: To study and compare the effects of aerobic physical training associated with the chronic cholinergic stimulation on autonomic and cardiovascular hemodynamic parameters in Spontaneously Hypertensive Rats (SHR).

Design and method: 96 rats (20 weeks) were divided into 4 groups: sedentary SHR (SED-H2O); sedentary SHR treated with pyridostigmine bromide (20mg/kg) (SED-PYR); SHR submitted to physical training by swimming (TRE-H2O); and SHR trained and treated with pyridostigmine bromide (TRE-PYR). The swimming occurred for 10 weeks, and the chronic cholinergic stimulation for 2 weeks with pyridostigmine bromide.
Polyethylene cannulae were inserted into the left femoral vein and artery of the animals in the end of the treatments, and, in this way, were analyzed using different approaches: 1) pharmacological evaluation of autonomic tonus 2) analysis of heart rate (HRV) and systolic arterial pressure variability (SAP); 3) spontaneous baroreflex sensitivity (BRS).

Results: SED-PYR group had a reduction of heart rate (HR) and mean arterial pressure (MAP) compared to SED-H2O group (322±6 vs. 355±4 bpm; 138±3 vs. 151±3 mmHg). In turn, TRE-H2O and TRE-PYR groups also had reduced HR and MAP (324±6 and 297±6 bpm; 140±4 and 130±5 mmHg, respectively) associated with a reduction in the intrinsic HR (325±6 and 322±5 vs. 340±3 bpm). Considering the autonomic parameters, the SED-PYR group presented an increased vagal tone and a reduction in variability of low-frequency oscillations in SAP. The group TRE-H2O presented similar autonomic responses to those in SED-PYR group, but also lower LF oscillations and an increase in high-frequency oscillations of HRV compared to the SED-H2O. Pyridostigmine bromide treatment in trained animals (TRE-PYR) showed higher prevalence of vagal tone in determining basal HR compared to other groups. However, it also presented higher LF oscillations and reduced HF oscillations of HRV. Additionally, baroreflex sensitivity did not differ between groups.

Conclusions: As observed with physical training, chronic cholinergic stimulation with pyridostigmine bromide reduced the MAP and improved some parameters of cardiovascular autonomic control. However, the association of both did not intensify the effects observed. Thus, further studies should be conducted to investigate the possible physiological mechanisms involved.

PP.05.35 EFFECTS OF DIFFERENT ANTIHYPERTENSIVE PHARMACOLOGICAL TREATMENTS ON THE CARDIOVASCULAR AUTONOMIC CONTROL EVALUATED BY DIFFERENT EXPERIMENTAL APPROACHES IN ANIMAL MODEL

K. Delgado Maida, S. Vieira, H.C. Dutra De Souza. *Biomechanics, Medicine and Rehabilitation, Program in Rehabilitation and Functional Performance, FMRP/USP, Ribeirão Preto, BRAZIL*

Objective: To study and compare the effects of different antihypertensive pharmacological treatments on the cardiovascular autonomic control in spontaneously hypertensive rats (SHR).

Design and method: Eighteen-week-old SHRs (N=36) were divided into different groups: control group (vehicle) and five groups treated for 10 weeks with the following antihypertensive drugs: Enalapril (ENL), Losartan (LOS), Hydrochlorothiazide (HCTZ), Propranolol (PRO) and Amlodipine (AML). The animals received daily doses of drugs diluted in drinking water. In the last week of treatment, polyethylene cannulae were inserted into the left femoral vein and artery for drug administration and measurement of heart rate and blood pressure, respectively. The animals were analyzed using different approaches: 1) pharmacological evaluation of autonomic tonus 2) analysis of heart rate (HRV) and systolic arterial pressure variability (SAPV); 3) spontaneous baroreflex sensitivity (BRS). For statistical analysis, Sigma-Stat® software was used.

Results: When compared to the vehicle group, all groups had reduced systolic blood pressure, however, only the ENL and LOS groups had significant reductions in diastolic blood pressure. In addition, the PRO group showed reduced basal HR (373 bpm+13 x 421+42 bpm), and the ENL group presented reduced intrinsic pacemaker HR (308 bpm+26 x 343+30 bpm).
The vehicle group showed sympathetic dominance in determining the basal HR, in contrast, the PRO group showed vagal dominance in determining the baseline HR when compared to the ENL, HCTZ and AML groups, considering that for these animals the chronotropic response after the administration of propranolol was significantly lower, when compared to the response obtained after the administration of methylatropine.
For HRV, the pharmacologically treated group showed no significant difference in the values of low frequency band and higher power in high frequency band, compared to the vehicle group. The analysis of systolic arterial pressure variability revealed that the ENL group showed a reduction in the LF band, compared to the vehicle, LOS, PRO and HCTZ groups.

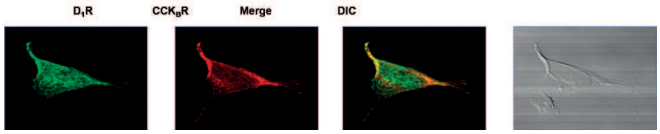
Conclusions: None of the pharmacological treatment was able to completely attenuate the adverse effects of hypertension on the autonomic parameters in spontaneously hypertensive rats, however, the group treated with Enalapril showed a positive effect on the SAPV.

PP.05.36 GASTRIN AND D1 DOPAMINE RECEPTOR INTERACT TO INDUCE NATRIURESIS AND DIURESIS

Y. Chen [1,2], L. Asico [3], S. Zheng [1,2], V. Villar [3], D. He [1,2], L. Zhou [1,2], C. Zeng [1,2], P. Jose [3]. *[1] Department of Cardiology, Daping Hospital, Third Military Medical University, Chongqing, CHINA, [2] Chongqing Institute of Cardiology, Chongqing, CHINA, [3] Division of Nephrology, Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA*

Objective: Oral NaCl intake produces stronger natriuresis and diuresis than venous infusion of same amount, indicating the existence of renal-gastric axis. Gastrin, from gastrointestinal tract, is dominant one due to its natriuretic effects and taken-up by the renal proximal tubule (RPT) cells. We hypothesize that gastrin interact with do-

pamine receptors in kidney, resulting in synergistically increased sodium excretion. The impaired interaction might be involved in hypertension.



Design and method: Wistar-Kyoto (WKY) rats, spontaneously hypertensive rats (SHR) and RPT cells were stimulated or blocked through D1-like dopamine and gastrin receptors to observe Na +-K +-ATPase activity and natriuresis.

Results: Gastrin infusing WKY rats via renal artery induced natriuresis and diuresis, which was blocked in the presence of CI988, a gastrin receptor blocker. Similarly, effect hereinbefore of fenoldopam, a D1-like receptor agonist, was blocked by D1-like receptor antagonist, SCH23390, indicating gastrin and fenoldopam play natriuretic and diuretic effect through individual receptors. Lower dosages of gastrin or fenoldopam failed to induce natriuresis and diuresis alone, while putting together induced the effects. The above-mentioned effects were lost in SHRs. Natriuresis and diuresis was partially blocked by SCH23390 or CI988, indicating the interaction between gastrin and D1-like receptor. Stimulation of either receptor increased the expression of the other and inhibited Na+-K+-ATPase activity, while the inhibitory effect of Na+-K+-ATPase activity was partially blocked through its corresponding receptors due to respective existence of SCH23390 and CI988.

Conclusions: It indicated the synergistic effect between gastrin and D1-like receptor would increase the sodium excretion in WKY rats; the impaired interaction might be involved in the pathogenesis of hypertension.

PP.05.37 OMACOR PROTECTS THE HEART OF MELATONIN-DEFICIENT SPONTANEOUSLY HYPERTENSIVE RATS (SHR) FROM MALIGNANT ARRHYTHMIAS

T. Benova [1], C. Viczenczova [1], J. Radosinska [2], B. Bacova [1], J. Zurmanova [3], V. Knezl [4], M. Zeman [5], B. Obsitnik [6], N. Tribulova [1]. *[1] Institute for Heart Research, Slovak Academy of Sciences, Bratislava, SLOVAK REPUBLIC, [2] Institute of Physiology, Medical Faculty, Comenius University, Bratislava, SLOVAK REPUBLIC, [3] Department of Physiology, Faculty of Science, Charles University, Prague, CZECH REPUBLIC, [4] Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences, Bratislava, SLOVAK REPUBLIC, [5] Faculty of Natural Sciences of Comenius University, Bratislava, SLOVAK REPUBLIC, [6] Abbott Laboratories, Bratislava, SLOVAK REPUBLIC*

Objective: Data from literature indicate that melatonin in addition to regulation of circadian rhythm exhibits antihypertensive, free radicals scavenging and antiarrhythmic effects as we have shown recently. While melatonin deficiency observed in pts suffering from CHD and hypertension as well as in SHR can contribute to disease progression and pro-arrhythmia. Continuous light suppresses melatonin production that is deleterious to the heart. We aimed to explore whether cardioprotective compound Omacor might be beneficial in these conditions.

Design and method: Males SHR and age-matched healthy Wistar rats were housed under standard 12h light/dark cycle or exposed to continuous light under 24h light/day for 6 weeks. Half of these rats received Omacor (omega-3 ethyl ester, 25g/kg diet). Left ventricular tissue was analyzed for mRNA of electrical coupling protein, connexin-43 (Cx43), proinflammatory NFkB and iNOS using real time PCR while protein expression of Cx43 and PKCε by western blots. Inducible ventricular fibrillation (VF) was examined using isolated-perfused heart.

Results: Comparing to healthy rats plasma levels of melatonin were lower in SHR. Continuous light caused mild elevation of BP in healthy rats and enhanced it in SHR and caused decrease of threshold to induce VF in both groups of rats comparing to rats under normal light cycle. Myocardial Cx43 mRNA level was not altered but Cx43 protein and its functional phosphorylated forms (which affect electrical coupling) were decreased in SHR due to continuous light and partially restored by Omacor. Treatment with Omacor also attenuated continuous light-induced increase of myocardial iNOS (which down-regulates Cx43) and proinflammatory NFkB gene expression as well as increased threshold for VF.

Conclusions: Findings indicate that continuous light-induced melatonin deficiency itself impairs myocardial Cx43 channels-mediated intercellular electrical coupling that may contribute to enhanced increased risk for malignant arrhythmias in hypertensive rats. These adverse effects can be, in part, eliminated by treatment with Omacor.

PP.05.38 PROTECTIVE EFFECT OF (-)-EPICATECHIN ON BLOOD PRESSURE, VASCULAR FUNCTION AND NITRIC OXIDE BIOAVAILABILITY IN SPONTANEOUSLY HYPERTENSIVE RATS

P. Balis [1], M. Galleano [2], A. Puzserova [1], C.G. Fraga [2,3], M. Kluknavsky [1], O. Pechanova [1], I. Bernatova [1]. *[1] Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, SLOVAK REPUBLIC, [2] Physical Chemistry, Institute of Molecular Biochemistry and Medicine, University of Buenos Aires, Buenos Aires, ARGENTINA, [3] Department of Nutrition, University of California, Davis, CA, USA*

Objective: This study investigated the antihypertensive effect of purified (-)-epicatechin (Epi) on blood pressure (BP) and vascular function of the femoral artery (FA) in adult (22-week) spontaneously hypertensive (SHR) rats.

Design and method: SHR males were divided into control group and Epi-treated group,Wistar-Kyoto (WKY) rats were used as a negative control (n=6 in each). Epi was administered six days in the daily dose approximately 250 mg/kg. BP was determined by tail-cuff plethysmography, nitric oxide (NO) synthase activity by conversion of [^{3}H] L-arginine in the aorta and vascular function (FA) using a wire myograph.

Results: Six-day administration of Epi reduced BP by about 13% and elevated aortic NO-synthase activity by about 173% in SHR, as compared to control ($p<0.05$). Noradrenaline-induced constriction of the FA was elevated in SHR vs. WKY and Epi partially normalized this parameter. Endothelium-dependent relaxation was evaluated using acetylcholine (ACh) test as the responses of serotonin (Ser, 1 μmol/l) pre-contracted preparations in the FA. ACh-induced relaxation of the FA was lower in SHR group than in the WKY group ($p<0.05$). Epi restored vascular function in SHR to the level observed in the WKY group. Interestingly, maximal ACh-induced endothelium-dependent relaxation of the FA was in Epi group significantly elevated compared to SHR and WKY ($p<0.05$). This improvement was associated with a significant elevation of NO-dependent component of ACh-induced relaxation. Sodium nitroprusside (SNP)-induced endothelium independent relaxation was similar in each groups.

Conclusions: In conclusion, dietary Epi reduced BP and improved vasorelaxation and NO synthase activity in genetically hypertensive rats by the increase of vascular NO bioavailability. Effect of Epi on blood pressure and vascular function indicates a promising use of Epi in nutritional or pharmacological procedures in the prevention and treatment of arterial hypertension in humans.

PP.05.39 INCREASED PROPENSITY OF HYPERTENSIVE RAT HEART TO MALIGNANT ARRHYTHMIAS IS RELATED TO LOWER OMEGA-3 INDEX

B. Bacova [1], C. Viczenczova [1], T. Benova [1], P. Sec [2], M. Certik [3], N. Tribulova [1]. *[1] Institute for Heart Research, Slovak Academy of Sciences, Bratislava, SLOVAK REPUBLIC, [2] Institute of Biochemistry and Genetic of Animals, Slovak Academy of Sciences, Bratislava, SLOVAK REPUBLIC, [3] Slovak University of Technology, Bratislava, SLOVAK REPUBLIC*

Objective: Low ω-3 index was suggested as a risk factor for cardiovascular diseases and sudden cardiac death. We have previously shown that hypertensive rats benefit from ω-3 fatty acid (FA) intake. Aim of this study was to explore relationship between ω-3 index and susceptibility of aged male and female spontaneously hypertensive rats (SHR) to ventricular fibrillation (VF).

Design and method: One year-old SHR and age-matched healthy Wistar rats (WR) fed with ω-3FA (Vesteralens, Norway, EPA+DHA 200mg/day/2month) were compared with untreated rats. Gas chromatography was used for analysis of red blood cells (RBC) ω-3FA composition: alfa-linolenic acid, eicosapentanoic acid (EPA), docosahexanoic acid (DHA) and ω-6FA composition: linoleic acid, arachidonic acid (AA), gama-linolenic acid. ω-3 index was calculated as RBC level of EPA + DHA expressed in percentage of total FA. Susceptibility of the heart to electrically induced VF was examined using Langedorff-perfused heart preparation.

Results: RBC levels of EPA and particularly DHA were lower in SHR than WR regardless the sex. Comparing to healthy WR ω-3 index was lower in both male and female SHR, i.e. 0.73% and 0.44% versus 1.75% and 1.17%. This parameter was significantly increased due to ω-3 FA intake to 2.38% and 3.34% in male and female SHR. Moreover, treatment was associated with a decrease in AA/EPA ratio in SHR. Non-treated male and female SHR were much prone to inducible VF (100% males and 65% females) comparing to WR (65% males and 35% females) but this propensity was significantly reduced to 35% in males and 25% in females SHR due to ω-3FA intake.

Conclusions: Results suggest an inverse relationship between ω-3 night index and susceptibility of hypertensive rats to VF.
This findings support the hypothesis that lower ω-3 index might be a marker of increased propensity of the heart to malignant arrhythmias.

PP.05.40 ESTRADIOL AND HYPOXIC PULMONARY HYPERTENSION IN FEMALE GONADECTOMIZED AND MALE WISTAR RATS

M. Artemieva [1], O. Maslova [2], D. Lozinskaya [2], Y. Kovaleva [2].
[1] M.V.Lomonosov Moscow State University, Department of Human and Animal Physiology, Biological Faculty, Moscow, RUSSIA, [2] M.V. Lomonosov Moscow State University, Department of Pharmacology, Faculty of Basic Medicine, Moscow, RUSSIA

Objective: The incidence of pulmonary arterial hypertension (PAH) among women of different ages greater than that among men (Pugh, Hemnes, 2010). Gender-dependent differences in the manifestation of PAH suggest involvement of sex hormones in these processes. Animal experiments revealed that chronic administration of estradiol (E2) both male and female rats with monocrotaline- and bleomycin-induced forms of PAH reduces development of this disease (Umar et al., 2012). The aim of current research was to investigate role of estradiol in developing of hypoxic PAH (hPAH) in male and female Wistar rats.

Design and method: White male and female gonadectomized Wistar rats were used. The procedures followed the FELASA/ICLAS for use of the laboratory animals (Guide for use of the laboratory animals, National Academy Press, Washington, D.C.1996). The rats were divided into 4 experimental groups, which were injected subcutaneously during 2 weeks with: 1,2-propandion (vehicle, 200mkl/rat/day (male and female rats)); E2 (15mkg/kg/day (female gonadoectomized rats) and 75mkg/kg/day (male rats)). Then half of experimental animals were exposed to hypobaric hypoxia. Rats were housed in a hypobaric chamber at simulated altitude of 5000m, 10h a day, 2wk. The other half of experimental animals was used as normoxic control.
Right ventricular systolic pressure (RVSP) and index (RV weight/(Left ventricular+Septum weight)) was measured as indication of PAH developing.

Results: Two weeks after hypoxia exposure male rats from hypoxic control and E2 groups developed PAH (the degree of RVSP and RV index was greater in hypoxic groups versus appropriate control). RVSP in hypoxic E2 group was tended to decrease versus hypoxic non-E2 group (p=0,08). In gonadoectomize female rats, RVSP increased only in hypoxic E2 group (versus normoxic E2 group (21,6%) and hypoxic non-E2 control (18,3%)). RV index was higher in both female hypoxic groups, but hypoxic E2 rats demonstrated significant increase of RV index compare with hypoxic non-E2 control (13,0%).

Conclusions: Estradiol seems to play protective role during developing of hPAH in male Wistar rats whereas in female gonadectomized Wistar rats estradiol injection led to significant amplification of hPAH symptoms (RVSP and RV index).

PP.05.41 ZINC DEFICIENCY DURING INTRAUTERINE AND POSTNATAL GROWTH INDUCES AORTIC MORPHOLOGICAL AND FUNCTIONAL ALTERATIONS IN RATS

C. Arranz, F. Mendes Garrido, N. Gobetto, L. Juriol, M. Dasso, G. Wenk, R. Elesgaray, C. Caniffi, A. Tomat. *Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Iquimiefa-Conicet, Buenos Aires, ARGENTINA*

Objective: Moderate zinc deficiency during intrauterine and postnatal growth induces an increase in blood pressure levels in adult males related to cardiovascular and renal disorders. To evaluate aortic morphology and function in adult male rats exposed to fetal and postnatal zinc deficiency.

Design and method: Female Wistar rats received during pregnancy up to weaning low (L:8 ppm) or control (C:30 ppm) zinc diet. After weaning, male offspring fed low (l) or control (c) zinc diet during 60 days (Cc, Ll, Lc). At day 81, we measured systolic blood pressure (SBP,mmHg, tail-cuff technique) and we evaluated the thoracic aorta morphology (Sirius red staining): artery area (Aa, mm2), media area/lumen area (Ma/La, %), collagen in tunica media (Fibrosis, arbitrary score, scale 0 to 4). In aorta we measured basal nitric oxide synthase (NOS) activity, and endothelial (eNOS), neuronal (nNOS) and inducible (iNOS) isoforms activities (pmol 14C-L-citrulline/g.tissue.min).
In aortic rings, suspended in Krebs solution and preconstricted with phenylephrine 10-5M, we evaluated the maximal relaxation (ACh Emax, %) with acetylcholine (10-10 to 10-3 M); we also measured the maximal contraction with angiotensin-II (Ang-II Emax, % maximal contraction with KCl 90mM, 10-10 to 10-6 M). Values are means±SEM, n=6/group. One way ANOVA, Bonferroni post-test.

Results:

	Cc	Ll	Lc
SBP	126±1	143±1*	146±2*
Aa	2.3±0.1	1.7±0.1*†	2.5±0.2
Ma/La	22.8±0.4	23.0±0.4	23.8±0.6
Fibrosis	1.1±0.6	3.1±0.3*	1.6±0.3
NOS activity	225±5	172±4*	160±8*
ACh Emax	90±1	76±5*	77±3*
Ang-II Emax	32±3	23±2*	25±2*

*p<0.01vs Cc; †p<0.01vs Lc.
Basal NOS activity was not affected by nNOS and iNOS inhibitors, but was decreased by blocking Ca2+-calmodulin (Cc:55±2#, Ll:64±1#, Lc:61±9#,#p<0.001 vs. basal) in all groups.

Conclusions: Zinc is an important micronutrient for arterial development and function. Moderate zinc deficiency during whole life is associated to a reduced aortic size with preserved Ma/La relation and higher signs of fibrosis in tunica media. Zinc deficiency during fetal and/or postnatal life programs a lower endothelial nitric oxide production that could explain the vascular hyporesponsiveness to ACh and an unexpected reduced contractile response to Ang-II probably due to alterations in Ang-II receptors in this model.

POSTERS' SESSION

POSTERS' SESSION PS06
HEART

PP.06.01 VALIDATION OF SERUM BIOMARKERS IN PATIENTS WITH SEVERE AORTIC STENOSIS AND HYPERTENSION

E. Zhiduleva, O. Moiseeva, P. Murtazalieva, E. Kazakova, O. Irtyuga, L. Korostovceva. *Federal Almazov Medical Research Centre, Saint-Petersburg, RUSSIA*

Objective: The aim of the study was to estimated role of osteoprotegerin/RANK/RANKL and hypertension in calcific aortic stenosis (AS).

	BAV, n=31	TAV, n=30	Control, n=31	p
OPG,pmol/l	6.2±0.5*	6.7±0.5**	4.85±0,3	*p=0.04 vs Ctrl **p=0.02 vs Ctrl
RANKL,pmol/l	0.48±0,03*	0.42±0,03	0.38±0,02	*p=0.008 vs Ctrl
HN, n (%)	22 (71)	28 (93)	0	
OBPs, mm Hg	135±3	141±4*	125±6	*p<0.05 vs Ctrl
OBPd, mm Hg	81±2	83±2	80±3	

OBPs – office systolic blood pressure; OBPd – office diastolic blood pressure

Design and method: Patients with peak aortic velocity (Vmax) more than 4.0 m/s were included. 61 pts with aortic valve stenosis (AS): 31 pts with bicuspid aortic valve (BAV) (57.3 ±1.0 yrs; m:f 1.8:1) and 30 pts with tricuspid aortic valve (TAV) (59.7 ±0.7 yrs; m:f 1:1) and 31 healthy persons as a control (57.6 ±0.8 yrs; m:f 1.1:1) were examined. Pts with infective endocarditis and rheumatic disease were excluded. Serum osteoprotegerin and sRANKL were performed in all pts by enzyme-linked immunosorbent assay.

Results: Patients with BAV and TAV were comparable for age, gender and ECHO parameters. Serum sRANKL and OPG levels weren`t different in groups with BAV and TAV. However serum concentration of OPG was increased in pts with TAV and BAV vs control group, while sRANKL level was increased in pts with BAV (tab.1). sRANKL concentration was correlated with office systolic and diastolic BP only in pts with TAV (r=0.4, p=0.02 and r=0.4, p=0.02 respectively). Whereas OPG concentration were negative correlated with office systolic BP in this group (r=-0.52, p=0.004). There wasn't correlation between BP and osteoprotegerin/sRANKL level in pts with BAV.

Conclusion: Systemic arterial hypertension is the key risk factor for OPG/RANKL/RANK system activation in pts without congenital heart disease. But traditional risk factor such as hypertension may contribute to the activation of OPG/RANKL/RANK system and progression of different etiology aortic stenosis.

PP.06.02 DECARTOGRAPHIC PARAMETERS OF REPOLARIZATION AS THE PREDICTORS OF RESPONSE TO ACUTE PULMONARY VASODILATOR TESTING IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

E. Yurasova, E. Blinova, T. Sakhnova, O. Arkhipova, N. Danilov, T. Martynyuk, I. Chazova. *Cardiology Research Complex, Moscow, RUSSIA*

Objective: To assess the possibilities of decartographic parameters of repolarization as the predictors of response to acute pulmonary vasodilator testing in patients with pulmonary arterial hypertension.

Design and method: 64 patients (mean age 41.4±12.4 years; 81% women) with pulmonary arterial hypertension who underwent right-heart catheterization and acute pulmonary vasodilator testing were evaluated. Digital orthogonal electrocardiograms were recorded and studied with the use of dipole electrocardiotopography (DECARTO). We studied the "recovery acceleration map", which shows the distribution of the dipole component of the depolarized state duration shortening over the heart surface. For a quantitative analysis the magnitude G (in ms) and spatial components Gx, Gy, Gz of the "recovery acceleration" vector (directed to the left, inferior, and anterior) were used.

Results: There were 24 responders (37.5%) to acute pulmonary vasodilator testing. Responders had lower mean pulmonary artery pressure (47.7±10.8 mm Hg versus 61.7±19.3 mm Hg, p <0.01), pulmonary vascular resistance (837±447 dyn•s/cm5 versus 1386±741 dyn•s/cm5, p <0.01), heart rate (69.7±10.6 bpm versus 82.0±13.6 bpm, p <0.01), and higher values of Gx (26.1±18.1 ms versus 5.9±19.1 ms, p <0.001) and Gy (26.7±16.9 ms versus 8.3±8.1 ms, p <0.001) as compared with non-responders. Receiver operating characteristic curve analysis identified an optimal cutoff value for Gx>8 ms to predict response, with sensitivity of 88% and specificity of 63% (the area under the ROC curve 0.78, SE 0.06) and cutoff value for Gy>14 ms with sensitivity of 75% and specificity of 88% (the area under the ROC curve 0.87, SE 0.05). There were more responders among patients with Gx>8 ms than with Gx<=8 ms (58% vs. 11%, p <0.001) and among patients with Gy>14 ms than with Gy<=14 ms (78% vs. 15%, p <0.001).

Conclusions: The use of repolarization process mapping by DECARTO technique may be helpful for predicting the results of pulmonary vasodilator testing in patients with pulmonary arterial hypertension.

PP.06.03 CARDIAC STRUCTURE AND FUNCTION IN RELATION TO HYPERTENSION SUBTYPES AND AMBULATORY BLOOD PRESSURES IN UNTREATED PATIENTS

T. Xu [1], F.H. Ding [2], J.J. Li [1], Y. Yan [1], F.F. Wei [1], L. Zhang [1], S. Wang [1], Y. Li [1]
[1] *Shanghai Institute of Hypertension Center for Vascular Evaluations, Shanghai, CHINA,* [2] *Ruijin Hospital, Department of Cardiology, Shanghai, CHINA*

Objective: Cardiac structural and functional abnormalities are well accepted cardiovascular risk factors. We aimed to investigate the association of cardiac structure and function with ambulatory hypertension subtypes and blood pressures (BP) in untreated patients.

Design and method: We enrolled consecutive untreated subjects referred to a hypertension clinic for the 24-hour ambulatory BP monitoring. In total, 656 patients (mean age, 50.9 years; 49.8% women) had both the ambulatory BP measured by SpaceLabs 90217 monitors and cardiac structure and function by echocardiography. Isolated diastolic hypertension (IDH), isolated systolic hypertension (ISH) and combined systolic and diastolic hypertension (SDH) were defined according to the thresholds of average ambulatory BP of 130 mmHg systolic and 80 mmHg diastolic. We used the analysis of variance to compare the cardiac parameters between groups, and the multivariate linear regression to analyze the association of cardiac structure and function with ambulatory systolic and diastolic BP.

Results: Compared to normotensive subjects (n=253), SDH patients (n=223) had larger left atrium diameter (LAD), left ventricular diastolic diameter (LVDD), left ventricular mass (LVM) and longer isovolumic relaxation (IVRT) (P<0.05), ISH patients (n=22) had higher LVM and E/E' ratio (P<0.05) after adjustment for sex, age, body weight, body height, plasma glucose, serum cholesterol, current smoking, alcohol intake, and heart rate. In simple correlation analysis, LVDD and LVM were significantly associated with both ambulatory systolic and diastolic BP (r=0.12-0.28, P<=0.002), whereas E/E' ratio was only associated with 24-hour systolic BP (r=0.10, P=0.01). In regression models including both systolic and diastolic BP and aforementioned covariables, LVM and E/E' ratio remained significantly related to 24-h systolic BP (P<0.05), but not diastolic BP in both younger (age<51 years) and older (age>=51 years) groups.

Conclusions: Ambulatory hypertension was associated with the changes in cardiac structure and function irrespective of the subtypes. Left ventricular mass and diastolic function was mainly determined by systolic BP in both young and older subjects.

PP.06.04 THE ROLE OF PRENATAL CHRONIC HYPOXIA ON MYOCARDIAL ISCHEMIA / REPERFUSION INJURY IN ADULT RABBITS OFFSPRING

Z. Wang, Z. Huang. *Cardiology Department, 2nd Affiliated Hospital of Fujian Medical University, Quanzhou, CHINA*

Objective: To evaluate the role of prenatal chronic hypoxia on myocardial ischemia/reperfusion injury in adult rabbits offspring and explore the relevant mechanism.

Design and method: The pregnant New-Zealand rabbits were divided randomly into normoxic (n=8) and hypoxic (12% O2 from days 10 to 28 of gestation, n=8) groups. One male offspring of each maternal rabbit was randomly selected to study. The offspring rabbits were subjected to heat stress (42°C for 15 min) at 6 months of age. After 24 h, left anterior decending branches were excised and subjected to ischemia for 30 min and reperfusion for 120 min. Cardiac histopathological observation was performed by light microscope. The expression of heat shock protein 70 (HSP70) in myocardium was detected by immunohistochemistry. Myocardial enzyme activity, apoptotic index and caspase-3 activity in myocardium were examined as well.

Results: Ischemia-reperfusion after heat stress pretreatment increased myocardial enzyme activity, apoptotic index and caspase-3 activity in prenatal chronic hypoxia rabbits (4720.31 ± 744.39 IU/L, 1849.13 ± 416.58 IU/L, 40.43 ± 5.03%, 12.43 ± 1.77 unit, respectively) when compared with control (3388.95 ± 532.43 IU/L, 1435.13 ± 92.08 IU/L, 34.40 ± 4.66%, 10.58 ± 1.42 unit, respectively). Heat stress pretreatment induced HSP70 significant expression in left ventricular myocardium was not observed in prenatal chronic hypoxia rabbits but in normoxic control rabbits.

Conclusions: Prenatal chronic hypoxia inhibits HSP70 synthesis in the heart of adult offspring in response to body heat stress, which might insult cardioprotection against ischemia-reperfusion injury.

PP.06.05 HOW OFTEN IS ARTERIAL HYPERTENSION AMONG PATIENTS IN SECONDARY PREVENTION OF SUDDEN CARDIAC DEATH PRESENT? PROFILE OF PATIENTS ADMITTED DUE TO IMPLANTATION OF CARDIOVERTER DEFIBRILLATOR

A. Vachulova [1], M. Svetlosak [1], H. Bou Ezzeddine [1], B. Vohnout [2], K. Hatalova [1], V. Bernat [1]. *[1] National Cardiovascular Institute, Bratislava, SLOVAK REPUBLIC, [2] Slovak Medical University, Bratislava, SLOVAK REPUBLIC*

Objective: The mortality reduction achieved by implantable cardioverter-defibrillators (ICD) in primary and secondary prevention of sudden cardiac death (SCD) are well known, and have been confirmed by many randomized trials. Many of these trials created the backbone of currently valid guidelines on primary and secondary prevention of SCD. Management of patients after the reverse SCD is still at the forefront of not only arrhythmologists, as well as cardiologists, internists, emergency physicians. The aim of this work was to evaluate the profile of patients after the reverse sudden cardiac death before ICD implantation.

Design and method: A retrospective analysis of all patients after the reverse of SCD consecutively admitted to our center in 2011-2012 that have underwent implantation ICD system.

Results: Patients from our center were 171, mean age (61±11.05 years), significant higher amount of men 145 (85.96%) vs 26 (14.04 %). Diagnosis of arterial hypertension was known in 152 (88.90%) patients. Mean blood pressure at the admittance was 128.71/86.7 mmHg. In ECHOKG parameters, the mean EF 39.26 % ± 10,43, distribution of patients by NYHA functional class NYHA was 27.65% 1 41.76% NYHA 2 and 17.1% NYHA 3 In 75.29% of patients was documented ventricular tachycardia, in 19.3% patients was ventricular fibrillation.

Conclusions: Analysis of patients after reversed sudden cardiac death proves that it is a heterogeneous group of patients. Arterial hypertension is not typical for this group of patients, in, although there are patients with heart failure based on hypertensive heart. Results of completed investigations contribute to improving the management of patients after the reverse sudden cardiac death.

PP.06.06 THE INFLUENCE OF LONG-TERM COMBINED THERAPY WITH ZOFENOPRIL PLUS INDAPAMIDE ON LEFT VENTRICULAR HYPERTROPHY AND DIASTOLIC DYSFUNCTION IN PATIENTS WITH MILD TO MODERATE HYPERTENTION

E. Ter-Stepanyants, L. Aleksanyan, A. Naghdalyan, A. Ordyan, T. Bayramyan *Yerevan State Medical University, Yerevan, ARMENIA*

Objective: To assess the influence of long term combined therapy with Zofenopril plus Indapamide on left ventricular diastolic dysfunction and hypertrophy in patients with mild to moderate arterial hypertension.

Design and method: This study included 54 hypertensive patients, 21 men and 33 women (mean age 58.5±6.2 years). Mean duration of hypertension was 7.2±5.2 years. Initial systolic blood pressure (SBP) – 157.9±13.4mmHg, diastolic blood pressure (DBP) – 97.6±6.8mmHg, heart rate - 84.4±2.7bpm. Left ventricular mass index (LVMI)>120g/m2 for men and >100g/m2 for women considered as left ventricular hypertrophy (LVH). Diastolic heart function was assessed by the following Doppler parameters: early (E) and late (A) peak velocities, E/A ratio, isovolumic relaxation time (IVRT) and deceleration time of early peak velocity (DT).
All patients were treated with Zofenopril 30 mg plus Indapamide 2.5mg once daily for 1 year after one-week washout period. Doppler echocardiographic parameters of diastolic function and left ventricular mass index were determined at baseline and every 3-month. Systolic and diastolic blood pressure and heart rate were measured every month. The relationship between parameters was established by Spearman correlation analysis, $p<0.05$ was considered statistically significant.

Results: After 1 year of the treatment LVMI was decreased from 134.4±5.5g/m2 to 115.1±3.3g/m2 ($p<0.001$), E/A ratio increased from 0.83±0.22 to 1.02±0.24 ($p<0.002$), shortened isovolumic relaxation time (IVRT) from 116±11ms to 98±10ms ($p<0.001$), and decreased deceleration time (DT) from 216±22ms to 187±18ms ($p=0.002$). SBP and DBP were reduced from 157.9±12.4 to 132.4±11.8mmHg ($p<0.001$) and from 97.6±6.8 to 83.6±6.8 ($p<0.001$).

Conclusions: The long-term combined therapy with Zofenopril plus Indapamide effectively controls SBP and DBP, significantly improves diastolic function and beneficially effects on LVH in patients with mild to moderate arterial hypertension.

PP.06.07 LEFT VENTRICULAR REMODELING AND ADENINE NUCLEOTIDES PATIENTS` WITH HYPERTENSIVE DISEASE AND TYPE 2 DIABETES MELLITUS

I. Sytina. *Kharkov National Medical University, Kharkov, UKRAINE*

Objective: To study the concentration of adenine nucleotides depending on the remodeling type of left ventricle (LV) in patients with hypertensive disease (HD) and diabetes mellitus (DM) type 2.

Design and method: 50 patients were examined (30 women and 20 men, age 59.5 [52; 63] years) with HD and DM type 2. Concentration of adenine nucleotides (adenosine triphosphate (ATP), adenosine diphosphate (ADP) and adenosine monophosphate (AMP) were studied in erythrocyte suspension.
All patients were conducted with echocardiography. The classification of A.Ganau. was used to diagnose the remodeling type of LV.

Results: In assessing the types of remodeling it was found that the normal geometry was observed in 14.3 % of patients, concentric remodeling in 23.8%, concentric hypertrophy - 45,2% and 16,7% persons were noted with eccentric hypertrophy. During the study of the level of adenine nucleotides - as a marker of hypoxia development, it was revealed that the highest rates of ATP -1.5 [1.49; 1.54] mmol / l, with minimum of AMP - 1.49 [1.45; 1.55] mmol / l, were typical to people with normal geometry of the heart, the group with concentric remodeling statistically was equal to the group with normal geometry of the heart, however, it was marked a little decrease of ATP at increase of concentration of AMP to 9% and ADP to 13%. The groups with hypertrophy myocardium were charactarized by statistically proved ($p<0,05$) decrease of concentration of ATP, in comparison with normal geometry at 21% in case of concentric hypertrophy and at 27% in case of eccentric hypertrophy at simultaneous increasing of level of AMP at 21% in patients with concentric hypertrophy and at 24% in patients with eccentric hypertrophy of LV.

Conclusions: In our study patients with HD and DM type 2 showed predominance of concentric hypertrophy and concentric remodeling of the LV. It was established that the concentric and eccentric hypertrophy of the LV myocardium is characterized by the development of energy-deficient states with significantly lower levels of ATP with significantly higher ADP and AMP in comparison with the normal geometry of the heart.

PP.06.08 EARLY DETECTION OF ASYMPTOMATIC LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN HYPERTENSIVE PATIENTS

A. Stevanovic [1], M. Dekleva [2], N. Paunovic [1], S. Trajic [3], R. Cvjetan [4], A. Simic [1]. *[1] Railway Health Care Institute, Belgrade, SERBIA, [2] University Clinical Center Zvezdara, Belgrade, SERBIA, [3] Dedinje Cardiovascular Institute, Belgrade, SERBIA, [4] Zemun Medical Centre, Belgrade, SERBIA*

Objective: Development of overt congestive heart failure (CHF) may be preceded by a phase of asymptomatic left venrticular systolic dysfunction.
The aim of this study was early detection of alteration in left ventricular systolic function.

Design and method: 120 hypertensive patients, with preserved ejection fraction (EF), were divided in three groups according LVDD: normal (n=40), abnormal relaxation (Grade I, n=37) and pseudonormal (Grade II, n=43).
Left atrial volume index (LAVI), left ventricular mass index (LVMI), left ventricular dimensions and volume inexes (LVEDV/BSA and LVESV/BSA) and EF were estimated by echocardiography. We measured coresponding velocities

from tissue Doppler at the level of the septal mitral annulus (Em;Am;Sm), including E/Em and tissue Doppler myocardial performance index (tMPI). The same measurements were repeated after three years.

Results: Close correlations were found between Sm and EF (r=0.349;p=0.0009), LVMI (r=-0.222;p=0.015), LVEDV/BSA (r=-0.317;p=0.0004) and LVESV/BSA (r=-0.472;p=0.0005).
Levels of LVEDV/BSA (89.3vs103.8vs101.7; p=0.009), LVESV/BSA (34.0 vs42.9vs44.0; p=0.0004), LVMI (104.3vs112.5vs123.0; p=0.0004), LAVI (32.0vs35.5vs44.5; p=0.0001) and MPI (61.7vs72.1vs76.3; p=0.036) progressively increased from the normal group through LVDD Grade I and II groups. Significantly different values of EF (63vs61vs59; p=0.003) and Sm (0.074vs0.067vs0.059; p=0.003) were obtained between groups too, but with progressively decrease from the normal group through LVDD Grade I and II groups. General linear model for repeated measures showed increase of LVEDV/BSA (F=50.009;p<0.001), LVESV/BSA (F= 34.258;p<0.001), LVMI (F=27.648;p<0.001), LAVI (F=17.083;p<0.001) and tMPI (F=35.842;p<0.001) during three years, with significant time difference, but withot significant difference between groups, these parameters enarged in all groups almost at the same manner. Sm also significantly changed during three years with significant time difference (F=128.24;p<0.001) and with significant difference between groups (F=4.597;p< 0,012), Sm decrease in all groups, but most expressed in LVDD Grade II group.

Conclusions: Left ventriculae EF was not sensitive indicator for the detection of subclinical systolic dysfunction, but decrease of Sm appeared as the first sign of systolic abnormalities following established diastolic dysfunction and was the clear reflection of LV remodeling process. This suggests that Sm may aid in the identification of patients at high risk for development of CHF who need preventive treatment.

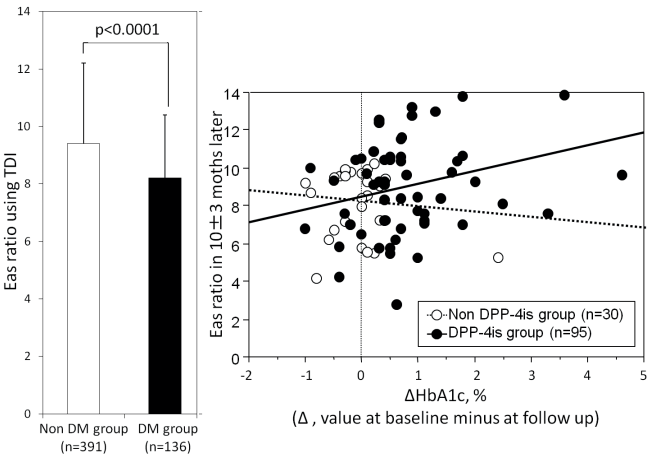
PP.06.09 AN ASSOCIATION BETWEEN DIPEPTIDLY PEPTIDASE-4 INHIBITORS TREATMENT AND LEFT VENTRICULAR STIFFNESS BY TISSUE DOPPLER IMAGING IN PATIENTS WITH TYPE 2 DIABETES

H. Sako, S. Miura, S. Furuyama, A. Matsunaga, K. Saku.
Department of Cardiology, Fukuoka University Hospital, Fukuoka, JAPAN

Objective: Left ventricular (LV) stiffness plays an important role in the pathogenesis of diastolic LV function. Since recent studies indicated that dipeptidly peptidase-4 inhibitors (DPP-4is) treatment might have non-glycemic beneficial effects, we estimated LV stiffness parameters of systolic and diastolic performance using tissue doppler imaging (TDI) in type 2 diabetes (T2DM) patients with or without DPP-4is treatment.

Design and method: This study enrolled 527 patients, 136 patients with T2DM were identified. In T2DM group, 55, 40 and 30 patients received sitagliptin, vildagliptin and non DPP-4is treatments for 10±3 months, respectively. We quantified Eas ratio, LV diastolic elastance index (Ed), arterial elastance index, LV end-systolic elastance index, ventricular-vascular coupling index, and total stiffness index (TSI).

Results: Ed (p<0.0001) and TSI (p<0.05) were significantly increased, and Eas ratio (p<0.0001) was significantly decreased in patients with T2DM. After DPP-4is treatment was associated with a stronger increase in Eas ratio. In addition, Eas ratio at follow-up was correlated with δHbA1c in DPP-4is group (r=0371, p<0.05), but non DPP-4is group. However, there were no significantly differences in LV stiffness parameters between sitagliptin and vildagliptin treatment.



Conclusions: The Eas ratio for evaluating LV stiffness was decreased in patients with T2DM, and increased after DPP-4is treatment.

PP.06.10 VOLUME OF CAROTID BODIES ESTIMATED BY COMPUTED TOMOGRAPHY ANGIOGRAPHY AND HEART RATE TURBULENCE IN PATIENTS WITH ESSENTIAL HYPERTENSION

P. Jazwiec [1], R. Poreba [2], P. Gac [1], M. Poreba [3], M. Jurdziak [2], G. Mazur [2], M. Sobieszczanska [3], *[1] 4th Military Hospital, Department of Radiology and Diagnostic Imaging, Wroclaw, POLAND, [2] Wroclaw Medical University, Department of Internal Medicine, Occupational Diseases and Hypertension, Wroclaw, POLAND, [3] Wroclaw Medical University, Department of Pathophysiology, Wroclaw, POLAND*

Objective: The study aimed at determination of a relationship between an estimated total volume of carotid bodies (V rCB+lCB), evaluated using computed tomography angiography (CTA) and heart rate turbulence (HRT) in patients with essential hypertension.

Design and method: The study was conducted on 32 consecutive patients with diagnosed and pharmacologically treated essential hypertension. In all the participants CTA of carotid arteries was performed with evaluation of carotid bodies (CB) volume as well as 24-hour Holter (ECG) monitoring with evaluation of heart rate turbulence. Volume of every carotid body was evaluated on the basis of scans obtained in CTA of carotid arteries, using the formula: 4/3 x π x transverse dimension of CB in axial projection x longitudinal dimension of CB in axial projection x craniocaudal dimension of CB in sagittal/frontal projection. In analysis of heart rate turbulence considered following parameters: turbulence onset (TO) and turbulence slope (TS). The analysed HRT indices allowed to define percentages of individuals with both normal parameters of HRT (HRT0), individuals with a single abnormal HRT parameter (HRT1) and individuals with both abnormal HRT parameters (HRT2).

Results: Mean values of TO were significantly higher while mean values of TS were significantly lower in the group of patients with essential hypertension manifesting V rCB+lCB values >= median value, than in the group of essential hypertension patients with V rCB+lCB values < median value (TO (%): -0.58 ± 0.51 vs. -1.67 ± 0.88; TS (ms/RR): 4.15 ± 1.81 vs. 6.71 ± 2.25; p<0.05). A significantly lower percentages of individuals with HRT0 was found in the group of essential hypertension patients with V rCB+lCB values >= median value than in the group of patients with essential hypertension manifesting V rCB+lCB values < median value (HRT0 (%): 57.1 vs. 92.9; p<0.05). Statistically significant linear relationships were demonstrated between V rCB+lCB on one hand and TO, TS on the other (correlation coefficient r: 0.47, -0.51).

Conclusions: In patients with essential hypertension an unfavourable relationship is noted between volume of carotid bodies, evaluated by CTA of carotid arteries, and heart rate turbulence.

PP.06.11 "PROTECTIVE" EFFECTS OF PREVIOUS ARTERIAL HYPERTENSION IN CARDIAC AL AMYLOIDOSIS

S. Perlini [1], F. Pietrangiolillo [1], E. Binot [1], R. Dell'Acqua [1], R. Mussinelli [1], A. Raimondi [1], F. Musca [1], F. Cappelli [2], F. Perfetto [2], F. Salinaro [1], M. Boldrini [1], G. Palladini [3], G. Merlini [3]. *[1] Clinica Medica II, Fondazione IRCCS San Matteo, University of Pavia, Pavia, ITALY, [2] Internal Medicine Department, University of Florence, Florence, ITALY, [3] Amyloidosis Research and Treatment Center and Department of Molecular Medicine, Fondazione IRCCS San Matteo, University of Pavia, Pavia, ITALY*

Objective: Cardiac AL amyloidosis is caused by extracellular deposition of fibrillar aggregates of insoluble toxic protein, mainly composed by the N-terminus of a monoclonal immunoglobulin light-chain. Given the high prevalence of arterial hypertension in the general population, a rare disease like cardiac AL amyloidosis may develop in a hypertensive patient.
Aim of the study was to assess whether previous (or current) cardiac exposure to increased blood pressure has an impact on cardiac structural and functional response to amyloid deposition and on the subsequent prognosis.

Design and method: Presence or absence of arterial hypertension was defined according to history, previous or current antihypertensive treatment in 165 consecutive untreated cardiac AL amyloidosis patients (age 64 ± 10 years). Serum NT-proBNP, cardiac troponin I (cTnI) and free light chains (dFLC) - i.e. the most robust prognosticators that have been demonstrated so far - were assessed, and echocardiography was performed at diagnosis in all patients.

Results: A positive history of arterial hypertension was reported in more than one third of cardiac AL patients (n=60/165; 36%). When comparing hypertensive

vs. non-hypertensive cardiac AL patients, no difference was observed either in the prevalence of extracardiac organ involvement or in structural/ biochemical variables that can estimate the severity of the disease-associated cardiac amyloid load, such as left ventricular mass index or serum NT-proBNP [169 (140-191) vs. 175 (137-199) vs g/m2; 5431 (2579–12229) vs. 5487 (2256–9818) pg/ml; p=ns for both]. In contrast with the extent of diastolic dysfunction, systolic function was much less impaired in hypertensive patients, as assessed by stress-corrected midwall fractional shortening and longitudinal excursion of the mitral annulus. At Kaplan-Meyer analysis, hypertension was a univariable predictor of patients' survival after a median follow-up of 561 days (p<0.0017). At multivariable analysis, high levels of NT-proBNP, of cTnI and hypertension resulted independent survival predictors, whereas elevated dFLC did not enter the model.

Conclusions: In cardiac AL patients, a previous history of arterial hypertension is accompanied by a different functional adaptation to amyloid deposition, favorably affecting overall survival. Previous hypertension predicts a better prognosis independent of high NTproBNP or high TnI.

PP.06.12 POSSIBLE DETERMINANTS OF LEFT VENTRICULAR MASS INDEX AND THEIR ASSOCIATION WITH GLUCOMETABOLIC STATUS: A CROSS-SECTIONAL STUDY

M. Pareek [1], M.L. Nielsen [1], M. Leósdóttir [2], R. Kruger [1,3], S.V. Greve [1], M.K. Blicher [1], D. Rujic [4], P. Hindersson [5], T. Sehestedt [6], K. Wachtell [7], P.M. Nilsson [8], M.H. Olsen [1,3]. *[1] Cardiovascular and Metabolic Preventive Clinic, Department of Endocrinology, CIMA, Odense, DENMARK, [2] Department of Cardiology, Skåne University Hospital, Malmö, SWEDEN, [3] Hypertension in Africa Research Team (HART), North-West University, Potchefstroom, SOUTH AFRICA, [4] Department of Internal Medicine, Odense University Hospital, Svendborg Hospital, Svendborg, DENMARK, [5] Department of Clinical Biochemistry, Holstebro Hospital, Holstebro, DENMARK, [6] Department of Cardiology, Herlev University Hospital, Herlev, DENMARK, [7] Department of Internal Medicine, Glostrup University Hospital, Glostrup, DENMARK, [8] Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, SWEDEN*

Objective: To explore possible determinants of left ventricular mass index (LVMI) and their association with glucometabolic status in middle-aged or older apparently healthy subjects.

Design and method: We examined cross-sectional associations between LVMI, markers of a) afterload (increased systolic blood pressure (SBP), N-terminal pro-brain natriuretic peptide (NT-proBNP), b) systemic inflammation (high-sensitivity C-reactive protein, interleukin 6, growth differentiation factor 15 (GDF-15)), c) fibrosis (procollagen type 1 N-terminal propeptide), and d) fasting plasma glucose (FPG) categorized as normal fasting glucose (NFG: FPG<=6.0mmol/L), impaired fasting glucose (IFG: FPG 6.1-6.9mmol/L) and diabetes mellitus (DM: FPG>=7.0mmol/L), in 524 men and 220 women aged 56-79 years without overt cardiovascular disease who received no cardiovascular, antidiabetic or lipid lowering drugs, using multiple linear regression analysis.

Results: In separate age- and sex-adjusted models, SBP (beta=0.22 (95% confidence interval (CI), 0.15-0.29; p<0.001), NT-proBNP (beta=0.18 (95% CI, 0.12-0.23); p<0.001), GDF-15 (beta=0.002 (95% CI, 0.000-0.004); p=0.045), and FPG category (beta=2.04 (95% CI, 0.06-4.02); p=0.04) were independently associated with LVMI. SBP (beta=0.008 (95% CI, 0.006-0.011); p<0.001) was significantly and positively associated with FPG category. In a subsequent model adjusted for age, sex, and FPG category, only SBP (beta=0.22 (95% CI, 0.14-0.29); p<0.001) and NT-proBNP (beta=0.17 (95% CI, 0.12-0.23); p<0.001) (adj. R2=0.176; p<0.001) remained independently predictive of LVMI. There was a significant interaction between GDF-15 and FPG category (NFG: beta=0.000 (95% CI, -0.003-0.002); IFG: beta=-0.003 (95% CI, -0.008-0.001); DM: beta=0.008 (95% CI, 0.004-0.013); p<0.001), but not between FPG category and SBP or FPG category and NT-proBNP. In patients with DM, only GDF-15 (beta=0.007 (95% CI, 0.004-0.011); p<0.001) and NT-proBNP (beta=0.17 (95% CI, 0.10-0.25); p<0.001) (adj. R2=0.176; p<0.001) were significantly associated with LVMI.

Conclusions: In a multiple linear regression model adjusted for age, sex, and FPG category, only markers of increased afterload, i.e. increasing SBP and NT-proBNP independently predicted LVMI. However, in patients with untreated DM, GDF-15 levels were also significantly associated with LVMI, suggesting a role for inflammation in the development of left ventricular hypertrophy in patients with DM.

PP.06.13 POSSIBLE MECHANISMS EXPLAINING THE DEVELOPMENT OF DIASTOLIC DYSFUNCTION IN PATIENTS WITH IMPAIRED GLUCOSE METABOLISM: A CROSS-SECTIONAL STUDY

M. Pareek [1], M.L. Nielsen [1], M. Leósdóttir [2], R. Kruger [1,3], S.V. Greve [1], M.K. Blicher [1], P. Hindersson [4], T. Sehestedt [5], K. Wachtell [6], P.M. Nilsson [7], M.H. Olsen [1,3]. *[1] Cardiovascular and Metabolic Preventive Clinic, Department of Endocrinology, CIMA, Odense, DENMARK, [2] Department of Cardiology, Skåne University Hospital, Malmö, SWEDEN, [3] Hypertension in Africa Research Team (HART), North-West University, Potchefstroom, SOUTH AFRICA, [4] Department of Clinical Biochemistry, Holstebro Hospital, Holstebro, DENMARK, [5] Department of Cardiology, Herlev University Hospital, Herlev, DENMARK, [6] Department of Internal Medicine, Glostrup University Hospital, Glostrup, DENMARK, [7] Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, SWEDEN*

Objective: To explore possible mechanisms explaining the association between impaired glucose metabolism and left ventricular diastolic dysfunction in middle-aged or older apparently healthy subjects.

Design and method: We examined cross-sectional associations between the presence of grade 2 or 3 diastolic dysfunction, markers of a) hemodynamic load (increased systolic blood pressure (SBP), left ventricular mass index (LVMI), and N-terminal pro-brain natriuretic peptide (NT-proBNP)), b) dyslipidemia (triglycerides, total cholesterol, low- and high-density lipoprotein cholesterol) and myocardial ischemia (high-sensitivity cardiac troponin T (hsTnT)), c) systemic inflammation (high-sensitivity C-reactive protein, interleukin 6, growth differentiation factor 15) and fibrosis (procollagen type 1 N-terminal propeptide), and d) fasting plasma glucose (FPG) categorized as normal fasting glucose (NFG: FPG<=6.0mmol/L), impaired fasting glucose (IFG: FPG 6.1-6.9mmol/L) and diabetes mellitus (DM: FPG>=7.0mmol/L), in 507 men and 215 women aged 56-79 years without overt cardiovascular disease who received no cardiovascular, antidiabetic or lipid lowering drugs, using binary logistic regression analysis.

Results: The prevalence of diastolic dysfunction increased significantly with worsening glucometabolic status (NFG: 13%; IFG: 15%; DM: 25%; chi-square 10.56, p=0.005). In separate age- and sex-adjusted models, SBP (exp(beta)=1.01 (95% confidence interval (CI), 1.01-1.02); p=0.004), LVMI (exp(beta)=1.02 (95% CI, 1.01-1.03); p<0.001), NT-proBNP (exp(beta)=1.01 (95% CI, 1.00-1.02); p=0.04), and hsTnT (exp(beta)=1.04 (95% CI, 1.01-1.07); p=0.02) were significantly associated with diastolic dysfunction. After further adjusting for FPG category, only SBP (exp(beta)=1.01 (95% CI, 1.00-1.02); p=0.02) or LVMI (exp(beta)=1.02 (95% CI, 1.01-1.03); p<0.001) remained independently predictive of the presence of diastolic dysfunction. There was a significant interaction between FPG category and SBP (NFG: exp(beta)=1.03 (95% CI, 1.01-1.05); IFG: exp(beta)=1.01 (95% CI, 0.99-1.03); DM: exp(beta)=1.00 (95% CI, 0.98-1.02); p=0.03), but not between FPG category and LVMI.

Conclusions: In a binary logistic regression model adjusted for age, sex, and FPG category, only markers of increased load, i.e. SBP or LVMI, independently predicted diastolic dysfunction. The importance of SBP decreased with increasing impairment of glucose metabolism suggesting additional other mechanisms than load, dyslipidemia, ischemia, inflammation, or fibrosis for development of diastolic dysfunction in DM.

PP.06.14 ASSESSMENT OF ELECTROCARDIOGRAPHIC AND ECHOCARDIOGRAPHIC LVH IN A GENERAL POPULATION IN NORTHERN ITALY

M. Salvetti, A. Paini, F. Bertacchini, G. Rubagotti, G. Maruelli, E. Colonetti, C. Agabiti Rosei, E. Casella, E. Agabiti Rosei, M.L. Muiesan.
Internal Medicine, University of Brescia, Brescia, ITALY

Objective: A large number of studies have demonstrated that left ventricular hypertrophy (LVH) detected with standard electro- and echocardiography is an independent predictor of future cardiovascular complications in various subsets of patients.
Due its low cost and wide availability electrocardiography represents the first line test for the assessment of cardiac organ damage in hypertensive patients.
However a significant limitation is represented by its low sensitivity in detecting LVH. Aim of this study was to evaluate the prevalence of LVH detected by electro- or echocardiography and the relationship between these two measures in a general population sample (Vobarno study).

Design and method: A total of 385 subjects (mean age 57±10years,44%males ,64%hypertensives,44% overweight and 16%obese)underwent clinical examination with blood pressure measurement, standard laboratory examinations, a 12 leads electrocardiogram standard and standard echocardiography. EKG-LVH was defined as the presence of a Sokolow-Lyon voltage>=38 mm and/ or a Cornell voltage QRS duration product>2440 mm*msec; Echo-LVH was defined as LVM>50 g/m2.7 in men and 47g/m2.7 in women.

Results: LVH prevalence was 5.1% and 16.3% with EKG and Echo, respectively. LVH was detected by both methods only in 2.0% of patients. The prevalence of EKG-LVH was 1.7% with Sokolow-Lyon voltage,4.2% with Cornell product and 5.1% with both EKG criteria. In hypertensives the prevalence of LVH was significantly greater than normotensives(6.8% vs 2.2% with EKG-LVH and 22.7% vs 9.6% with Echo).The concordance of the two techniques in identifying patients with LVH was only partial, and in particular, among patients with EKG-LVH a significant proportion(39%) did not have echo-LVH. However, patients with EKG-LVH but without Echo-LVH had greater LV mass index(39.9 vs 34.4 gr/ m2.7,p<0.01)and worse systolic and diastolic function (midwall fractional shortening:17.3 vs 19.5; E/Em 10.6 vs 8.1,all p<0.01)as compared with those without both EKG and Echo-LVH.A positive correlation was observed between LVMI and Sokolow-Lyon voltage (r=0.13,p<0.015), Cornell product (r=0.22,p<0.001), Cornell voltage (r=0.45,p<0.001) and R in Avl (r=0.38,p<0.001).

Conclusions: Our data confirm the greater sensitivity of echocardiography examination for detection of LVH. The presence of EKG-LVH is associated with greater LVMI and worse systolic and diastolic function, even in the absence of clear-cut echo-LVH. Our results confirm the importance of identifying cardiac organ damage with both methods for a better stratification of cardiovascular risk.

PP.06.15 MIXOMA ATRII SINISTRI: CASE REPORT

M. Otljanska. *University Clinic of Cardiology, Skopje, FYROM*

Objective: Primary cardiac tumors represent a relatively rare diagnosis with autopsy frequency of only 0,001-0,03%,in which myxoma is the most commom type. Cardiac myxoma is usually solitary and develop in the atria,75% origina ting in the left atrium and 15%-20% in the right atrium .Women are more commonly affected, between third and sixth decades. The clinical features of myxomas are determined by location. size and mobility. Surgical extirpation is considered to be the tretament of choice.
In the present case we describe a asymtomatic patients in which diagnosis of mixoma is accidently discover.

Design and method: We present a clinical case of 50 year old female patient with mild to moderate hypertension, with non regulate blood pressure beside antihypertensive treatment. We performed several investigations during hospitalization: blood chemistry electrocardiograms (EKG), transtoracic echocardiography (TTE). transesophageal echocardiography (TEE), telecordis, and coronary angiography (CA).

Results: Biochemical parametars were normal, with normal EKG -sinus rithm with HR-75,without abnormalites of AV-conduction or ST segment. Telecordis was normal. TTE which is performed show Tu formation (34x26) in left atrium (42mm) with nonhomogenic structure and litlle calcification in the structure with a small stalk which attaches to the interatrial septum without obstruction or prolapse into the ventricule. TEE confirm the diagnosis of Tu formation in left atrum and a presense of litlle Tr in left atrum appendics. CA was performed with normal coronary artery. Patient was send to cardiosurgery centar ,and the mass was surgically removes with patch closure of the discontinuty of interatrial septum. Histological examination reveales mixoma cordis.
Three months later a routine contol TTE was performed and it was normal.

Conclusions: Mixoma cordis may present with cardiovascular related or constitutional symtoms, but sometimes a cardiac mass is discover incidentally during a imaging examination performed for an unrelated indication. Because of nonspecific symtoms early diagnosis may be a challenge.

PP.06.16 LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN ASYMPTOMATIC BLACK HYPERTENSIVE SUBJECTS

D. Ojji [1], S. Ajayi [2], M. Mamven [3], M. Ngabea [1], K. Sliwa [4].
[1] Cardiology Unit, Dept. of Medicine, University of Abuja Teaching Hospital, Gwagwalada, Abuja, NIGERIA, [2] Nephrology Unit, Dept. of Medicine, University College Hospital, Ibadan, NIGERIA, [3] Nephrology Unit, Dept. of Medicine, University of Abuja Teaching Hospital, Gwagwalada, Abuja, NIGERIA, [4] Hatter Institute of Cardiovascular Research in Africa, University of Cape Town, Cape Town, SOUTH AFRICA

Objective: Although hypertension has been established to be one the commonest causes of heart failure especially in sub-Saharan Africa, few data are available on the prevalence of asymptomatic left ventricular systolic dysfunction in a population sample of hypertensive subjects, especially in high risk groups such as blacks. The present study was therefore undertaken to assess the prevalence of asymptomatic left ventricular systolic dysfunction in hypertensive black African subjects.

Design and method: 1947 hypertensive subjects without heart failure presenting to the Cardiology Unit, Department of Medicine, University of Abuja Teaching Hospital from April 2006 to August 2013 had clinical and echocardiography evaluation.

Results: 953(48.9%) were male and 994(51.1%) were female. 93.3% had normal left ventricular systolic function (left ventricular ejection fraction (LVEF) > 54%), 4.4% had mild left ventricular systolic dysfunction (LVEF between 40-54%) and 2.3% had severe left ventricular systolic dysfunction (LVEF < 40%). Male subjects had worse left ventricular systolic function compared to women (LVEF of 73.2% versus 75.6%, p-value < 0.0001) and diabetic subjects had worse left ventricular systolic function compared to non-diabetic subjects (LVEF of 72.3% versus 75.7%, p=0.02). In regression analysis, lower left ventricular ejection fraction as continuous variable was associated with older age (r= 0.43, p< 0.0001), elevated serum creatinine level (r=0.16, p=0.02) higher relative wall thickness (r=2.2, p=0.02) and higher left ventricular mass index for height (r = 11.8, p< 0.0001). It was also associated with lower pulse pressure (r=3.2, p< 0.001), lower mean arterial pressure (t=2.3, p=0.02) and lower body mass index (r=5.3, p< 0.0001).

Conclusions: In a cohort of asymptomatic Black hypertensive subjects, up to 6.7% had left ventricular systolic dysfunction, and left ventricular systolic dysfunction was related to male gender, elevated serum creatinine, higher left ventricular mass, higher relative wall thickness and diabetes mellitus.

PP.06.17 THE ASSOCIATION OF UNCONTROLLED HYPERTENSION WITH CORONARY ARTERY CALCIUM SCORE, LEFT VENTRICULAR HYPERTROPHY, AND LEFT VENTRICULAR STRAIN

M.L. Nielsen [1], M. Pareek [1], S.V. Greve [1], S.Z. Diederichsen [2], R. Kruger [1,3], M.K. Blicher [1], M.H. Sørensen [2], H. Mickley [2], A.C. Diederichsen [2], M.H. Olsen [1,3]. *[1] Cardiovascular and Metabolic Preventive Clinic, Department of Endocrinology, CIMA, Odense, DENMARK, [2] Department of Cardiology, Odense University Hospital, Odense, DENMARK, [3] Hypertension in Africa Research Team (HART), North-West University, Potchefstroom, SOUTH AFRICA*

Objective: To examine the association between hypertension and coronary artery calcium (CAC) score, electrocardiographic left ventricular hypertrophy (LVH), and electrocardiographic strain pattern.

Design and method: We conducted a modified case-control study in which 36 women and 19 men aged 19-80 years with uncontrolled hypertension (office systolic blood pressure (SBP) >= 140 mmHg and/or diastolic blood pressure >= 90 mmHg with or without antihypertensive treatment) and no cardiovascular disease (CVD) or diabetes mellitus (DM) were matched 1:2 (matching factors: age, sex, smoking status, body mass index (BMI)) with subjects from a randomly selected cohort of men and women either 50 or 60 years old without CVD or DM, and evaluated for differences in CAC (Agatston score), LVH (Sokolow-Lyon index (SLI) or Cornell voltage-duration product (CVDP)), and strain (Minnesota criteria). Between-group differences were tested using independent samples t-test or Pearson's chi-squared test, and the associations were further evaluated using multiple linear or binary logistic regression.

Results: CAC (170 vs. 32; p=0.02), SLI (27 vs. 18; p<0.001), and CVDP (2318 vs. 1544; p<0.001) were significantly higher in patients with uncontrolled hypertension than in controls. CAC > 99 (29% vs. 11%; p=0.006) and LVH (41% vs. 6%; p<0.001), but not CAC > 0 (51% vs. 37%; p=0.1) and strain (14% vs. 11%; p=0.7), were significantly more prevalent in hypertensive patients. After adjusting for age, gender, smoking status, SBP, heart rate, total cholesterol, high-density lipoprotein cholesterol, BMI, waist circumference, the use of lipid-lowering drugs, and number of antihypertensive drugs, uncontrolled hypertension remained independently predictive of CAC (beta=125 (52-198); p=0.001), SLI (beta=9.24 (6.76-11.72); p<0.001), CVDP (beta=625 (409-840); p<0.001), CAC > 99 (exp(beta)=3.68 (1.28-10.54); p=0.02), and LVH (exp(beta)=10.15 (3.91-26.35); p<0.001). When predicting CAC, there was a significant interaction between patient group and total cholesterol (uncontrolled hypertension: beta=-97 (-205-9); controls: beta=-10 (-31-10); p=0.03), and patient group and BMI (uncontrolled hypertension: beta=31 (10-51); controls: beta=1 (-3-6); p<0.001), respectively. No significant group-related interactions were detected in the prediction of SLI or CVDP.

Conclusions: The presence of uncontrolled hypertension was independently associated with higher values of CAC and a greater prevalence of electrocardiographic LVH.

PP.06.18 DETERMINANTS OF LEFT VENTRICULAR MASS IN RENAL TRANSPLANT RECIPIENTS

L. Lakkas [1], K.K. Naka [1], E. Dounousi [2], V. Koutlas [2], I. Gkirdis [1], A. Bechlioulis [1], D. Evangelou [1], F. Zarzoulas [2], A. Kotsia [1], O. Balafa [2], G. Tzeltzes [1], G. Nakas [1], K. Pappas [1], R.G. Kalaitzidis [2], C.S. Katsouras [1], L.K. Michalis [1], K. Siamopoulos [2].
[1] University of Ioannina, Department of Cardiology, Ioannina, GREECE,
[2] University of Ioannina, Department of Nephrology, Ioannina, GREECE

Objective: Renal transplantation (RT) has been associated with a decrease in left ventricular mass (LVM) compared to pre-transplantation. However, little is known regarding the factors that may affect LVM after transplantation. The aim of the study was to identify determinants of LVM index (LVM adjusted to body surface area) in RT recipients (RTR).

Design and method: Forty-five RTR (mean age 50 years, 67% males, median time from RT 59 months) who attend the out-patient RT clinic of an academic hospital participated in the study. No patient had known cardiovascular disease. Conventional 2D and tissue Doppler echocardiography was used to assess cardiac function. Coronary flow reserve (CFR) in the left anterior descending artery using dipyridamole was also measured. Multivariate linear regression models were constructed using all variables that reached statistical significance at $p<0.1$ level in univariate correlation with LVM index.

Results: Hypertension and diabetes were reported in 87% and 16% of our population respectively. Thirty-one patients (69%) were previously on hemodialysis and the remainder on peritoneal dialysis. Triple immunosupression regime (calicineurin inhibitor based) was administered in 87% of RTR while the rest 13% of patients received a steroid-free, double regime. LV hypertrophy was found in 49% of patients. LVM index was associated with greater LV end-diastolic volume, stroke volume and left atrium size ($p<0.05$ for all). Increased systolic blood pressure, pulse pressure and time from transplantation, diabetes, and hemodialysis modality were all associated with greater LVM index ($p<0.05$ for all). LVM index was not related to CFR. In multivariate analysis, higher pulse pressure (B 1.16, $p<0.001$) and increasing time since transplantation (B 0.13 per month, $p=0.004$) were independent predictors of LVM index (R^2 0.41, $p<0.001$).

Conclusions: In conclusion, in RTR LVM index was associated with greater pulse pressure indicating the role of increased arterial stiffness. Furthermore, increased time from the transplantation procedure also predicted increased LVM. The role of stricter cardiovascular risk factor and blood pressure control, especially with increasing time since transplantation, on cardiac function remains to be elucidated in future studies.

PP.06.19 EFFECTIVENESS AND TOLERABILITY OF COMBINED THERAPY WITH ZOFENOPRIL AND LERCANIDIPINE IN ELDERLY PATIENTS WITH ISOLATED SYSTOLIC HYPERTENSION AND LEFT VENTRICULAR HYPERTROPHY

A. Naghdalyan, A. Aleksanyan, E. Ter-Stepanyants, A. Ordyan, T. Bayramyan.
Yerevan State Medical University, Yerevan, ARMENIA

Objective: This study aimed to evaluate the efficacy and tolerability of combined therapy with Zofenopril and Lercanidipine in elderly patients with isolated systolic hypertension (ISH) and left ventricular hypertrophy (LVH).

Design and method: 50 elderly patients (24/26 f/m) with ISH were studied during 32 weeks. Mean age of patients was 75.3±4.3 years. Mean duration of hypertension was 8.4±5.1 years.
All patients received Zofenopril 30mg and Lercanidipine 10-20 mg once daily for 32 weeks. Left ventricular mass, E/A ratio, left ventricular (LV) diastolic diameter, posterior wall and septal thickness were determined by EchoCG and Doppler examination at baseline and after 4 and 8 month of the treatment. Control examination of SBP and DBP were made every 2 weeks. Tolerability evaluations were based on adverse events, clinically relevant reports of abnormalities, laboratory tests, and patients requested to subjectively estimate their state, as excellent, good, satisfactory and unsatisfactory. The relationship between parameters was established by Spearman correlation analysis, $p<0.05$ was considered statistically significant.

Results: A distinct decrease in the level of SBP was noted already to the 2nd week from the beginning of the treatment. After 32 weeks SBP decreased from 168.2±15.8 to 134.4±10.5 ($p<0.001$). EchoCG and Doppler examination revealed reducing of LVMI from 133.6±4.4g/m2 to 114.5±3.1g/m2 ($p<0.005$), LV posterior wall and septal thickness reduced from 11.2±1.5 to 10.4±1.2 mm ($p<0.001$) and 12.65±1.15 to 11.2±1.4mm ($p<0.001$), E/A ratio increased from 0.78±0.17 to 0.86±0.14 ($p<0.002$). In the observed patients pulse pressure against the background of treatment by Zofenopril and Lercanidipine was reduced in 32 weeks by 40% of the initial level. Treatment was well tolerated; no clinically relevant or laboratory tests changes were induced by the treatment. None of the patients estimated his state as unsatisfactory.

Conclusions: This study shows that combined therapy with Zofenopril and Lercanidipine beneficially affects on left ventricular hypertrophy and blood pressure in elderly patients with isolated systolic hypertension, has a good tolerability and favorable effect on pulse pressure.

PP.06.20 LIPID PARAMETERS AND LEFT VENTRICULAR MASS IN ESSENTIAL HYPERTENSIVE PATIENTS

G. Mule', E. Nardi, C. Nardi, G. Geraci, R. Riccobene, L. Guarino, A.C. Foraci, G. Cerasola, S. Cottone. *European Hypertension Society Excellence Centre, University of Palermo, Palermo, ITALY*

Objective: Conflicting data exist about whether dyslipidemia plays a part in the development of ischemia-independent hypertensive heart disease. Moreover, little is known about the potential influence of gender on this relationship. Our aim was to assess the relationship of serum lipids with left ventricular (LV) mass in essential hypertensives (EHs).

Design and method: We enrolled 724 EH patients (mean age: 45 ± 12 years; 63 % males), free from cardiovascular complications and not treated with hypolipidemic drugs. In the patients previously pharmacologically treated for hypertension, treatment was withdrawn for at least 2 weeks. In all subjects total cholesterol (Tchol), serum triglycerides (TG) and HDL cholesterol (HDLc), were determined. Moreover, echocardiographic examination and 24-h ambulatory blood pressure (BP) monitoring, were performed. LV mass was indexed for body surface area (LVMI).

Results: In the overall population, and in men and women separately analysed, we did not observe any significant correlation of Tchol, LDLc and nonHDLc with LV mass. We found significant correlations of HDLc ($r = - 0.14$, $p < 0.0005$) and of TG ($r = 0.11$; $p = 0.003$) with LVMI. Similar results were obtained in both sexes. The TG/HDLc ratio showed significant correlations with LVMI in the overall population ($r = 0.16$; $p < 0.0005$), in women ($r = 0.15$, $p = 0.03$), and in men ($r = 0.15$, $p = 0.002$). When, in multiple regression models exploring the independent correlates of LVMI, HDLc and TG were both included as explanatory variables, only HDLc remained associated with LVMI ($\beta = - 0.108$, $t = -2.83$; $p = 0.0005$). When in the same models, instead of TG and HDLc, we added the TG/HDLc ratio, the association of this with LVMI was highly significant ($\beta = 0.14$, $t = 3.7$; $p < 0.0001$).
Analysis of the interaction term "gender x TG/HDLc" revealed no significant effect of sex on the association of TG/HDLc with LVMI.

Conclusions: Our results seem to suggest that among serum lipids only HDLc and the TG/HDLc ratio are related to LVMI. Insulin resistance might be the link between these parameters.

PP.06.21 CORONARY PERFUSION AND BLOOD PRESSURE IN SHIFT WORKERS

I. Mozos [1], E. Mozos [2], L. Filimon [3]. *[1] Victor Babes University of Medicine and Pharmacy, Department of Functional Sciences, Timisoara, ROMANIA,*
[2] Private Medical Office Dr. Mozos Emilian, Timisoara, ROMANIA, [3] Military Hospital, Department of Occupational Medicine, Timisoara, ROMANIA

Objective: To assess the relationship between blood pressure values and coronary perfusion in shift workers.

Design and method: A total of 47 shift workers (2-4 shifts), aged 31±8 years, 32% male, underwent arteriography. Systolic and diastolic blood pressure (SBP and DBP), systolic blood pressure in the aorta (SBPAo), mean arterial pressure (MAP), diastolic reflection area (DRA) and diastolic area index (DAI) were measured.

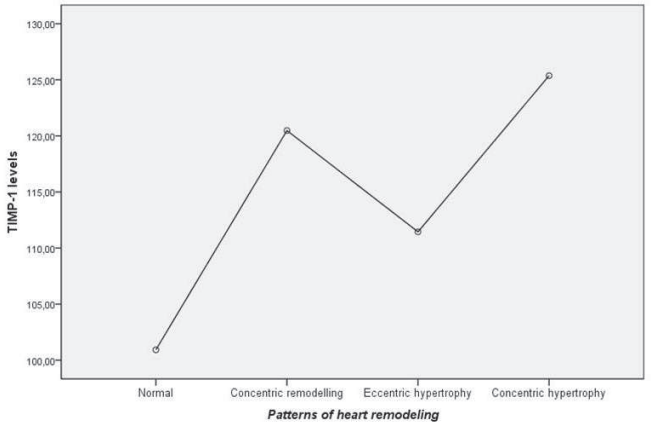
Results: Coronary perfusion was impaired in 47% of the participants. SBP, DBP, SBPAo, DRA and DAI were: 120±13 mmHg, 69±14 mmHg, 110±15 mmHg, 53±12 and 51±4.27%, respectively. Significant negative correlations were found between DAI and MAP (r=-0.313) and SBP (r=-0.311), respectively. Linear and multiple regression analysis revealed significant associations between blood pressure values, the number of shifts and DRA and DAI. DAI was significantly associated with the SBP ($p=0.032$) and DBP ($p=0.01$) (multiple $R=0.99$, R square=0.981, adjusted $R=0.957$, significance $F<0.01$). Significant associations were also found between impaired coronary perfusion (DRA<50 or/and DAI<50 % and elevated blood pressure values. Impaired DRA was significantly associated with elevated SBP ($p=0.016$) and the number of shifts ($p<0.01$).

Conclusions: Impaired coronary perfusion is associated with high normal blood pressure and hypertension in shift workers. Detection and control of high normal blood pressure and hypertension could represent effective preventive tools for coronary heart disease in shift workers.

PP.06.22 SERUM MATRIX METALLOPROTEINASE-1/TISSUE INHIBITOR OF MATRIX METALLOPROTEINASE-1 AND HEART REMODELING IN HYPERTENSIVE PATIENTS

M. Gómez [1], P. Morillas [1], A. Garcia-Honrubia [1], M. Ahumada [1], G. De Lara [1], V. Pernias [1], M. Sanchez [1], M. Sebastian [1], F. Garcia De Burgos [1], M. Portolés [2], M. Rivera [2], V. Bertomeu-Martínez [3]. *[1] Hospital General Universitario de Elche, Elche, SPAIN, [2] Cardiocirculatory Unit, Research Center, Hospital Universitario La Fe, Valencia, SPAIN, [3] Hospital Clínico Universitario San Juan, Alicante, SPAIN*

Objective: Increasing experimental evidence indicates that alterations in the extracellular matrix are implicated in hypertension and its chronic complications. The aim of our study was to determine if the plasma concentrations of matrix metalloproteinase-1 (MMP-1) and its tissue inhibitor (TIMP-1) are correlated with heart remodeling in arterial hypertension.



Design and method: We studied 159 consecutive patients with treated essential hypertension. An exhaustive evaluation of heart with echocardiography was performed to determinate left ventricular mass index (LVMI) and relative wall thickness (RWT), and plasmatic levels of MMP-1 and TIMP-1 were determined. Patients were categorized in four groups based in LVMI and RWT: 1) Normal geometry (58 patients); 2) concentric remodeling (54 patients); 3) concentric hypertrophy (42 patients); and 4) eccentric hypertrophy (5 patients).

Results: The mean age of hypertensive patients was 56 ± 13 years, with 67.3% male, 45.3% had dyslipidemia, 30% were diabetic and 27.7% smokers. 87.4% of patients were treated with antihypertensive drugs. In the comparative study, we observed that patients with ventricular hypertrophy (concentric and eccentric) and concentric remodeling had significantly higher plasma levels of TIMP-1 that patients with normal geometry (figure). There were no differences in MMP-1 levels. Furthermore a positive correlation between plasma levels of TIMP-1 and LVMI was found ($r = 0.326$, $p < 0.01$).

Conclusions: Our study shows higher plasma levels of TIMP-1 in patients with left ventricular hypertrophy and in those with concentric remodeling compared with hypertensive patients with structurally normal heart. TIMP-1 may have a role as a biomarker of heart remodeling in hypertensive patients.

PP.06.23 DETERMINANTS OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN HYPERTENSIVE PATIENTS

O. Matova, L. Mishchenko, S. Pavlenko. *SI-NSC «Institute of Cardiology named after M.D.Strazhesko» NAMS, Department of Essential Hypertension, Kiev, UKRAINE*

Objective: To identify risk factors related to left ventricular (LV) diastolic dysfunction in hypertensive patients without the diagnosis of congestive heart failure and with normal systolic function.

Design and method: One hundred fifty eight patients were underwent tissue Doppler imaging (TDI) and M-mode and Doppler echocardiography transmitral and pulmonary venous flow, measurement of fasting and postprandial immunoreactive insulin concentration on 60 and 120 min of standard oral glucose-tolerance test (OGTT). Blood pressure (BP) was measured by ambulatory BP monitoring. Mean age of patients was 57.2±2.4 years, average duration of hypertension was 16.6±2.9 years, mean body mass index (BMI) was 28.7±0.3 kg/m^2.

Results: One hundred six (67%) showed LV diastolic dysfunction (grade I and II diastolic dysfunction) on Doppler echocardiographic studies. Patients with LV diastolic dysfunction were older than those without LV diastolic dysfunction. After adjusting for age and sex, BMI was higher, hypertension duration was longer, BP and LV mass index, plasma insulin concentration on 60 and 120 min of OGTT was higher in patients with LV diastolic dysfunction than in those without LV diastolic dysfunction. In order to determine risk factors affect LV diastolic parameters we selected E/e' and TDI parameters e'/a', e', a'. In model were included age, duration of hypertension, BMI, BP, LV mass index and relation wall thickness, LV posterior wall thickness and interventricular septum thickness and plasma insulin concentration. Multiple regression analysis demonstrated that predictor of E/e' was age (ß=0.383, p=0.009), predictor of e'/a' was interventricular septum thickness (ß=-0.579, p=0.0001), predictor of e' was diastolic blood pressure (ß=-0.515, p=0.0001), predictor of a' was relation wall thickness (ß=-0.309, p=0.013).

Conclusions: Abnormalities in LV diastolic function in hypertensive patients without the congestive heart failure were associated with age, increase of diastolic blood pressure and with the development and progression of concentric LV hypertrophy.

PP.06.24 INCREASED CIRCULATING MESENCHYMAL STEM CELLS IN PATIENTS WITH ESSENTIAL HYPERTENSION AND LEFT VENTRICULAR HYPERTROPHY

M. Marketou [1], F. Parthenakis [1], N. Kalyva [1], C. Pontikoglou [2], S. Maragkoudakis [1], E. Zacharis [1], A. Patrianakos [1], F. Maragkoudakis [1], H. Papadaki [2], P. Vardas [1]. *[1] Cardiology Dept. Heraklion University Hospital, Heraklion, GREECE, [2] Hematology Dept. Heraklion University Hospital, Heraklion, GREECE*

Objective: Stem and progenitor cells are implicated in ventricular remodelling and have great clinical significance in many cardiovascular diseases. However, there are limited data regarding the involvement of mesenchymal stem cells (MSCs) in the pathophysiology of arterial hypertension. The aim of this study was to investigate the circulation of MSCs in patients with essential hypertension.

Design and method: We included 24 patients with untreated essential hypertension and 19 healthy individuals. All subjects underwent a complete echocardiographic study. In addition, peripheral blood samples from all participants were immunostained with antibodies against the cell surface markers CD34, CD45 and CD90. Using flow cytometry, we measured MSCs as a population of CD45-/CD34-/CD90+ cells and also as a population of CD45-/CD34-/CD105+ cells. The resulting counts were translated into the % percentage of MSCs in the total cells of peripheral blood.

Results: Hypertensive patients were shown to have increased circulating CD45-/CD34-/CD90+ compared to controls (0.0069 ± 0.012% compared to 0.00085 ± 0.0015%, respectively, p=0.039). No statistically significant difference in circulating CD45-/CD34-/CD105+ cells was found between hypertensives' and normotensives' peripheral blood (0.018 ± 0.013% compared to 0.015 ± 0.014%, respectively, p=0.53). Notably, CD45-/CD34-/CD90+ circulating cells were positively correlated with left ventNricular mass index (LVMI) (r=0.516, p<0.001).

Conclusions: Patients with essential hypertension have increased circulating MSCs compared to normotensives, and the number of MSCs is correlated with LVMI. Our findings contribute to the understanding of the pathophysiology of hypertension and might suggest a future therapeutic target.

PP.06.25 INTERACTION OF BLOOD PRESSURE LEVEL AND AGE ON HEART RATE VARIABILITY AND HEART RATE TURBULENCE IN ELDERLY HYPERTENSIVE PATIENTS

Z. Liu, Y. Zhao, H. Song, Y. Diao, H. Zhang. *Institute of Basic Medicine, Shandong Academy of Medical Sciences, Jinan, CHINA*

Objective: To investigate the interaction of blood pressure (BP) level and age on heart rate variability (HRV) and heart rate turbulence (HRT) in elderly hypertensive patients.

Design and method: Six hundred and ten participants were eligible enrolled in health examination center affiliated to Shandong Academy of Medical Sciences. Participants were divided into four groups, namely, aged 60 or over hypertensive group (n = 155), aged 60 or over nomortensive group (n =142), aged less than 60 hypertensive group (n =162), and aged less than 60 nomortensive group (n =151) according to BP level and age. Using Century 3000 Holter system, following parameters of HRT were assessed: SDNN, SDANN, square rMSSD, pNN50, VLF, LF, HF, and LF/HF ratio. The parameters of HRT were assessed as follows: TS and TO.

Results: In aged 60 or over hypertensive group, for parameter of HRV, SDNN was 71.6±21.5ms, SDANN was 65.4±16.0ms, rMSSD was 21.2±5.4ms, pNN50 was 30.5±9.8%, VLF was 597±193ms2, LF was 571±175ms2, HF was 169±69ms2, and LF/HF ratio was 3.5±1.2; for parameter of HRT, TS was 5.0±1.1ms/RR and TO was0.2±0.8%. In aged 60 or over hypertensive group SDNN, SDANN, rMSSD, pNN50, VLF, LF, HF, and TS were significant lower, and LF/HF and TO were significant higher than those in the other 3 groups ($P < 0.005$). In aged less than 60

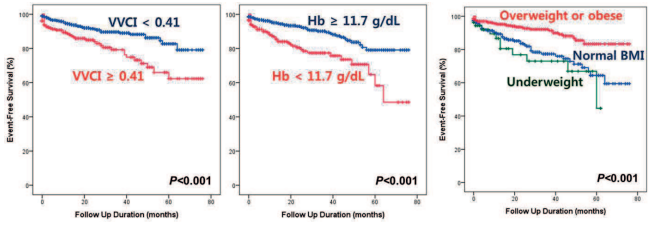
nomortensive group, SDNN, SDANN, rMSSD, pNN50, VLF, LF, HF, and TS were markedly higher, and LF/HF and TO were markedly lower than those in aged 60 or over nomortensive group and aged less than 60 hypertensive group (all P < 0.05). Either BP level or age significant impacted on heart rate variability and heart rate turbulence (P < 0.05).There were synergistic effects of BP level and age on SDNN, SDANN, rMSSD, VLF, LF, HF, LF/HF, TO, and TS (all P < 0.05).

Conclusions: BP level and age have synergistic effects on cardiac autonomic nervous dysfunction in elderly patients with hypertension.

PP.06.26 GLOBAL HEMODYNAMIC LOAD AS A PROGNOSTICATOR IN AORTIC STENOSIS

J. Lee [1], G. Cho [2], M.C. Cho [1]. *[1] Chungbuk National University Hospital, Cheongju, SOUTH KOREA, [2] Seoul National University Bundang Hospital, Seongnam, SOUTH KOREA*

Objective: Valve area and global hemodynamic load are important predictors of adverse outcome in aortic stenosis (AS). However, only limited data have been available to provide risk stratification. We evaluated whether ventriculo-vascular coupling index (VVCI) can be used as a prognosticator reflecting systemic hemodynamic load.



Design and method: A total of 848 consecutive asymptomatic patients (mean age, 71±12) with mild to moderate AS (aortic jet velocity >2.0 m/s) were retrospectively analyzed. We excluded the patients who have aortic valve area <1.0 cm² or ejection fraction <50%. Cardiovascular death, aortic valve replacement and admission for heart failure were regarded as clinical events.

Results: During mean follow up duration of 23±21 months, 40 patients were died from cardiovascular cause, 25 patients experienced aortic valve replacement and 31 patients were admitted with heart failure. Estimated event-free survival was 93.0 ± 1.0% at 1 year, 86.0 ± 1.6% at 3 years, and 75.7 ± 3.0% at 5 years. In multivariate Cox regression analysis, VVCI turned out to be the most powerful predictor of clinical events (adjusted HR 5.39, [95% CI 1.85-15.66], P=0.002). The patients with higher VVCI (>=0.41; the best cut-off value in ROC analysis) experienced clinical events more frequently (8.3% vs. 16.6%; OR 2.2 [95% CI 1.40-3.43], P<0.001). BMI (adjusted HR 0.89 [95% CI 0.82-0.96], P=0.003), hemoglobin (adjusted HR 0.87 [95% CI 0.77-0.99], P=0.037) and peak aortic jet velocity (adjusted HR 1.76 [95% CI 1.18-2.62], P=0.006) were also independent predictor of outcome.

Conclusions: The actual cardiovascular event rate of mild to moderate AS is substantially high in real world. In addition to conventional parameters, BMI, hemoglobin and VVCI are also powerful independent predictors of clinical events in asymptomatic mild to moderate AS.

PP.06.27 BLOOD PRESSURE PROFILE IN PATIENTS WITH OBSTRUCTIVE AND NONOBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY

F. Hashieva [1], A. Demkina [1], N. Krylova [1], E. Kovalevskaya [2], N. Poteshkina [1]. *[1] Pirogov Russian National Research Medical University, Moscow, RUSSIA, [2] Clinical City Hospital 52, Moscow, RUSSIA*

Objective: There are few studies focused on blood pressure (BP) profile in patients with hypertrophic cardiomyopathy (HCM) and influence of obstruction on BP parameters. To assess difference in BP profile and arterial stiffness in patients with obstructive and nonobstructive HCM.

Design and method: We examined 12 patients: 7 patients (group I) with obstructive HCM (4 men, average age 56.6±6.5 years) and 5 patients (group II) with nonobstructive HCM (2 men, average age 57.9±16.9 years). 24-h BP monitoring («BPLab») with arterial stiffness and central BP assessment were performed after therapy has been withdrawn. Two groups were comparable in gender (p=0.34), age (p=0.64), clinical status (II functional class by NYHA p=0.58) and arterial hypertension degree (2.3±0.5 and 2.4±0.5, p=0.88).

Results: There were no significant differences between I and II groups in maximum systolic BP (SPB) (171.6±15.7 and 165.6±11.2, p=0.53 accordingly), maximum diastolic BP (DPB) (106.9± 20.4 and 102.0±10.9, p=0.99), minimum SPB (104.0±12.2 and 99.0±8.6, p=0.52), minimum DPB (57.4±10.6 and 45.4±10.0, p=0.15), average daytime SBP (134.3±13.9 and 128.4±16.7, p=0.43), average daytime DBP (81.3±10.0 and 73.2±8.04, p=0.27), daytime SBP and DBP time index (p=0.43 and p=0.27 accordingly). Significant differences were revealed in average nighttime SBP (134.6±18.9 and 111.2±6.3, p=0.005), nighttime SBP time index (54.4±40.5 and 6.8±9.5, p=0.03) and nighttime SBP variability (14.7±7.0 and 9.2±2.0, p=0.04). In group I these parameters were higher. In group I SBP non-dippers were prevaled (43%) and in group II - dippers (40%), although the differense was not statisticaly significant (p=0.4). Ambulatory arterial stiffness index (AASI) was higher in group I (0.57±0.15 and 0.30±0.2, p=0.03). Significant correlation was revealed between obstruction and average nighttime SBP (r=0.79, p=0.002), nighttime SBP time index (r=0.66, p=0.02), nighttime SBP variability (r=0.62, p=0.03) and AASI (r=0.66, p=0.02).

Conclusions: Obstruction of LV outflow tract in HCM patients was associated with higher night SBP parameters and higher ambulatory arterial stiffness index.

PP.06.28 PREVALENCE AND PATTERN OF HIV-RELATED CARDIAC DYSFUNCTION AMONG NIGERIAN PATIENTS

G. Isiguzo [1], M. Iroezindu [2], B. Okeahialam [3]. *[1] Federal Teaching Hospital, Abakaliki, NIGERIA, [2] College of Medicine, University of Nigeria Enugu Campus, Enugu, NIGERIA, [3] Jos University Teaching Hospital, Jos, NIGERIA*

Objective: Human immunodeficiency virus (HIV) infection has added to the ever increasing list of causes of cardiovascular morbidity and mortality especially in the era of highly active antiretroviral therapy (HAART). We determined the prevalence and pattern of cardiac dysfunction among Nigerian HIV-infected patients.

Design and method: The study involved two hundred consecutively recruited HIV-positive consenting adults 18 years and above. It was questionnaire based, followed by clinical examination, laboratory investigations, electrocardiography (ECG), two dimensional echocardiography and Doppler studies.

Results: The mean age of the participants was 37±9 years and 71% were women. The median CD4 cell count was 358 cells/mm3 and 84.4% were on HAART. HIV-related cardiac dysfunction (HRCD) was diagnosed in 39.5%. HRCD was more common in males (52% vs. 35%, p-value 0.01) and in patients with CD4 cell <200 cells/mm3 (72% vs. 29%, p-value <0.001). Left ventricular hypertrophy was the most common ECG abnormality (29.6%). Diastolic dysfunction and systolic dysfunction each was seen in 10.5%, pericardial effusion in 8.5% with a case of tamponade, dilated cardiomyopathy 4.5%, isolated left ventricular dilatation 4.0%, pulmonary hypertension 4.0%, and right ventricular dysfunction 0.5%. Ejection fraction (p<0.01), fractional shortening (p<0.01) and left ventricular internal diameter (p<0.01) differed significantly between patients with HRCD and those without.

Conclusions: Cardiac disease complicating HIV/AIDS is common and various patterns exist. Considering the consequences of late diagnosis for cardiac disease in the light of its increasing burden in an immune-compromised population, we recommend regular cardiovascular screening for high risk groups in order to institute early intervention.

PP.06.29 CENTRAL AUGMENTATION PRESSURE IS INDEPENDENTLY RELATED TO MYOCARDIAL CONTRACTION AND RELAXATION

H. Gu [1], H. Fok [1], B. Jiang [1], M. Sinha [1], J. Simpson [2], P. Chowienczyk [1]. *[1] Clinical Pharmacology Department, King's College London, London, UNITED KINGDOM, [2] Paediatric Cardiology Department, Evelina London Children's Hospital, London, UNITED KINGDOM*

Objective: Central augmentation pressure (AP), an important component of central pulse pressure may be influenced by ventricular dynamics. We examined whether AP relates to myocardial contraction and relaxation independently of age, gender and left ventricular (LV) geometry in subjects with a wide range of blood pressure.

Design and method: We studied 120 subjects, evaluated for hypertension but otherwise free of clinically apparent cardiovascular disease aged 48.9±16.6 (mean ± SD) years with mean systolic blood pressure of 137.3±24.0 mmHg. Carotid pressure, obtained by tonometry calibrated from peripheral mean and diastolic BP, was used to calculate AP (difference between the second and first systolic peaks of the aortic waveform). Systolic (S) and diastolic (E') basal lateral segment velocities were measured by pulsed-wave Tissue Doppler Imaging, and early mitral inflow velocity (E) was measured by pulsed-wave Doppler from apical 4-chamber view. LV geometry was determined by LV mass over LV end diastolic volume (LVM/LVEDV) ratio.

Results: Augmentation pressure increased as the S wave decreased: 7.8±1.6,

13.0±1.6 and 16.2±1.7 mmHg (means±SE) for third, second and first tertiles of the S wave respectively (p=0.002) and increased as E/E' increased: 6.9±1.3, 11.9±1.2 and 18.2±2.1 mmHg for first, second and third tertiles of E/E', respectively (p<0.0001). After adjustment for age, gender and LVM/LVEDV, augmentation pressure was negatively associated with the S wave (standardized β=-0.31, p=0.001) and positively associated with E/E' (standardized β=0.35, p<0.0001).

Conclusions: Higher AP is associated with diminished longitudinal systolic contraction and impaired diastolic function independently of age, gender and LV geometry. These results do not determine the direction of causality between AP and ventricular dynamics but are consistent with ventricular dynamics being a determinant of AP.

PP.06.30 LOW DIASTOLIC BLOOD PRESSURE WAS ONE OF THE INDEPENDENT PREDICTORS OF ISCHEMIA-LIKE FINDINGS OF ELECTROCARDIOGRAM IN PATIENTS WHO UNDERWENT CORONARY ANGIOGRAPHY

S. Fujishima, T. Takiguchi, Y. Nakate, E. Nyuta, S. Kaseda, T. Koga, T. Tsuchihashi
Steel Memorial Yawata Hospital, Kitakyushu, JAPAN

Objective: To investigate whether low diastolic blood pressure (DBP) causes myocardial ischemia or not, the authors examined the relationship between DBP and ischemia-like findings of ECG.

Design and method: We enrolled 187 patients who underwent coronary angiography (CAG). Patients with conditions affecting ECG (e.g., patients taking digitalis or those with old myocardial infarction, complete right bundle branch block, or hypokalemia) were excluded from the analyses. Ischemia-like ECG was defined as having one or more of the following: borderline Q wave (Minnesota code (MC) I-3), ST depression (MC IV-1, 2, 3), negative T wave (MC V-1, 2, 3), and complete left bundle branch block (MC VII-1). CAG findings, blood pressure and other cardiovascular risks were analyzed to determine the significant factors for ischemia-like ECG.

Results: Based on the above definition, 70 of 187 patients (37%) had ischemia-like ECG. Compared with the group without it, the group with ischemia-like ECG included more females (p<0.01), and had lower values of body mass index (p=0.01), DBP (p<0.01), estimated glomerular filtration rate (p<0.01), left ventricular ejection fraction (LVEF, p<0.01), and higher values of age (p<0.01) and left ventricular mass index (LVMI, p<0.01). The severity of coronary artery disease did not differ between the groups. Receiver operating characteristics (ROC) curve analysis revealed that 74.5mmHg was the optimal cut-off point of DBP to predict ischemia-like ECG (area under curve, 0.63; 95% confidence interval, 0.55-0.71, p=0.003). There were no significant relationships between systolic blood pressure or severity of coronary artery stenosis and ischemia-like ECG. A multivariate analysis showed that female sex, low DBP (= or < 74.5 mmHg), LVMI, and EF were the significant factors for the ischemia-like ECG. The odds ratio of low DBP was 2.53 (95% confidence interval, 1.19-5.40; p=0.02).

Conclusions: Low DBP was one of the significant predictors of the ischemia-like ECG in the present study. Myocardial ischemia may be a part of the cause of high cardiovascular morbidity in the population with low DBP.

PP.06.31 LEFT VENTRICULAR DIASTOLIC STIFFNESS ASSESSED BY DIASTOLIC WALL STRAIN WITH CONVENTIONAL ECHOCARDIOGRAPHIC STUDY: CLINICAL AND EXPERIMENTAL OBSERVATIONS

I. Ennis, D. Broda, C. Massarutti, O. Pinilla, E. Escudero
Centro de Estudios Cardiovasculares, La Plata, ARGENTINA

Objective: The purpose of this investigation is to evaluate left ventricular diastolic wall strain (dws) based on the linear elastic theory, by echocardiography, in hypertensive patients (HT) and in spontaneously hypertensive rats (SHR).

Design and method: 15 consecutive HT and 15 normotensive (NT) for the same community and 24 rats, 8 normotensive (W) and 16 SHR: 8 controls and 8 treated (SHR T) with cariporide were studied. Echocardiography was performed in humans and animals to evaluate left ventricular (LV) structure and function. Dws was calculated according to Takeda et al. (J Cardiac Fail 2009;15:68-77). All the rats were sacrificed to weigh the heart, to measure the cross-sectional area of the myocytes, the fractional volume of collagen and the LV papillary muscle distensibility.

Results: LV mass index (LVMI) was higher (NT: 58,.89 ± 3.34 g/m2 ; HTA: 102.13± 8.6 g/m2, - p<0.01) and Dws was lower (NT: 0.46 ± 0.02, HTA: 0.38 ± 0.03- p<0.02) in HT; besides SHR also showed higher LVMI (W: 1.46±0.04 mg/g; SHR 2,31±0,15 mg/g – p< 0,01) with bigger size of myocytes (W: 285.26±18.47 m2, SHR: 447.38±36.94m2-p< 0,05), fractional volume of collagen (W: 2,50±0,30%, SHR:8,50±0,29%- p<0,05), worse papillary muscle distensibility (W: 0,013 ± 0,002 g/mm, SHR: 0,078 ± 0,0154 g/mm, p<0,05), and lowest Dws (W: 0,52± 0,01, SHR: 0,32±0,02- p<0,05). SHRT had LVMI (SHR-T: 1,59±0,14 mg/g, p<0,05), myocytes size (SHR-T: 287,32±20,52m2-p<0,05), and fraction volume of collagen (SHR T: 1,20±0,30%, p<0,05) reduction with improvement of papillary muscle distensibility (SHR-T: 0,010 ± 0,0021 g/mm - p<0,05) and Dws (SHR-T: 0,42±0,03% -p<0,05).

Conclusions: The analyzed results allow conclude that the utilization of an index of easy obtaining with transthoracic conventional echocardiogram, be effective to characterize the state of rigidity of the LV in human and animals model with arterial hypertension. This concept can be important to advance in the knowledge of the mechanisms that conduct to heart failure in this scenario.

PP.06.32 PREVALENCE OF PULMONARY HYPERTENSION IN PATIENTS WITH DEGENERATIVE MITRAL VALVE DISEASE IN ENUGU SOUTH-EAST NIGERIA

E. Ejim, C. Ubani-Ukoma, B. Onwubere
University of Nigeria Teaching Hospital, Ituku-Ozalla, NIGERIA

Objective: Pulmonary hypertension is a common complication of degenerative mitral valve disease, and contributes significantly to both morbidity and mortality. The use of medications for reduction of pulmonary pressure in patients is not a common practice by most physicians in this part of the world because of the absence of data on pulmonary hypertension. The authors set out to find the prevalence of pulmonary hypertension in patients with degenerative heart diseases and to determine if there are gender differences in affectation. This will form a basis for future research on the treatment of pulmonary hypertension in Sub-Saharan Africa.

Design and method: The echocardiographic records of 1390 patients done over a 4-year period were retrospectively reviewed. The examinations were done with a Logic 500MD Echocardiographic machine. Tricuspid valve regurgitant velocity above 250cm/s defined pulmonary hypertension. Data obtained included presence of degenerative mitral valve disease, pulmonary hypertension, age and gender.

Results: A total of 1390 echocardiogram reports done at Conquest Medical Imaging, Enugu, from July 2009 to August 2013 were retrospectively reviewed. Degenerative mitral valve disease was noted in 260 patients (18.7%), made up of 150 males and 110 females with a mean age of 68.3±14.4 years. Pulmonary hypertension was present in 75 patients (28.8%). There was no statistically significant difference in the frequency of pulmonary hypertension by gender.

Conclusions: Pulmonary hypertension is common in patients with degenerative mitral valve disease in Enugu, and both males and females are affected equally.

PP.06.33 BETA-AGONISTS WITH DIFFERENT TIME OF ACTION IN PATIENTS WITH CARDIOVASCULAR AND BRONCHO-OBSTRUCTIVE DISEASES

Y. Dolgusheva [1], K. Zykov [1], B. Nazarov [1], O. Agapova [2], L. Ratova [1], E. Shedrina [1], L. Luticova [1], G. Ryabykina [1], I. Chazova [1]. *[1] Russian Cardiology Research Complex, Moscow, RUSSIA, [2] Moscow State University of Medicine and Dentistry named after A.I. Evdokimov, Moscow, RUSSIA*

Objective: To evaluate the influence of beta-agonists with different time of action (short-acting, long-acting, ultra-long-acting) in patients with cardiovascular and bronchoobstructive diseases on blood pressure (BP) levels, heart rate (HR), ST-T changes, Qt/QTc changes.

Design and method: 30 patients with cardiorespiratory diseases (arterial hypertension and chronic obstructive pulmonary disease or bronchial asthma) were prospectively enrolled. All patients were examined initially. In the next three month patients were treated with 3 types of beta-agonists: at the 1st month – with salbutamol, at 2nd month –with formoterol, at 3rd month –with indacaterol. At the end of each month all patients underwent Holter monitoring recording and ambulatory blood pressure 24-monitoring. Results are presented as Mean±std.

Results: Patients were 64,36±6,5y.o., with BMI 29,6±4,8 kg/m2; Systolic BP 132,7±13,7 mmHg; Diastolic BP 83,1±10,4 mmHg. Baseline, 1-month, 2-month, 3-month BP, HR levels were similar among all patients (p=NS). During one month of treatment with ultra-long-acting beta-agonist QTc was lower than initially (421±25,9 vs 435±20,9, p=0,01). In contrast treatment with short-acting and long-acting beta-agonists caused no significant QTc change (421±25,9 vs 423,8±30,6, p=NS, 421±25,9 vs 430,5±33, p=NS, respectively).

Conclusions: Treatment patients with cardiorespiratory diseases by beta-agonists with different time of action during one month had not influence on blood pressure levels, heart rate, ST-T changes. However, treatment of patients by ultra-long-acting beta-agonists accompanied by reducing of QTc, which needs further investigations.

PP.06.34 TWELVE YEARS PROGNOSTIC SIGNIFICANCE OF ELECTROCARDIOGRAPHIC LEFT VENTRICULAR HYPERTROPHY IN PATIENTS WITH ARTERIAL HYPERTENSION

D. Djordjevic [1], I. Tasic [1], B. Stamenkovic [1], S. Kostic [1], M. Lovic [1], D. Marinkovic [1], D. Lovic [2], B. Lovic [2]. *[1] Institute Niska Banja, Nis, SERBIA, [2] Inter Medica, Dr. Lovic, Nis, SERBIA*

Objective: The aim of the study was to examine twelve years prognosis in patients (pts) with positive Lyon-Sokolow score and Cornell voltage QRS duration product and presence of echocardiographic left ventricular hypertrophy (LVH).

Design and method: We examined 104 pts (61 male and 43 female; mean age 55.3 ± 8.4 years) with echocardiographic LVH. The LVH cutpoints were 125 g/m² for male and 110 g/m² for female. Electrocardiographic LVH was defined as the presence of Lyon-Sokolow score (LS) > 38 mm and Cornell voltage QRS duration product (CP) > 2.440 mm*sec. The clinical and laboratory examination, electrocardiography, echocardiography, exercise testing, and 24-hours ambulatory blood pressure monitoring were done.

Results: Average left ventricular mass index (LVMI) was 170.8 ± 32.1 g/m² and duration of hypertension was 12.5 ± 7.7 years. During twelve years of follow-up in 31 (29.8%) pts occurred cardiovascular and cerebrovascular adverse events (ACE = myocardial infarction, cardiac or sudden death, angina pectoris, cerebrovascular insult). At the beginning of the study pts with ACE had greater: LVMI (190.4 ± 38.0 g/m² vs. 162.5 ± 25.2 g/m²; p < 0.001). Patients with ACE had greater QTc interval dispersion than patients without ACE (73.1 ± 19.7 ms vs. 54.0 ± 19.6; p < 0.001). There were positive correlations between LVMI and LS (r = 0.367; p < 0.01) and CP (r = 0.357; p < 0.01). ACE occurred in 9 (60.0%) pts of 15 pts with positive LS, and in 22 (24.7%) pts of 89 pts with negative score (odds ratio 4.57; 95% CI 1.46 to 14.28). ACE occurred in 11 (61.1%) pts of 18 pts with positive CP and in 20 (23.2%) pts of 86 pts with negative product (odds ratio 5.19; 95% CI 1.78 to 15.14).

Conclusions: Patients with echocardiographic LVH and positive LS and/or CP have additional risk for new cardiovascular adverse events than patients without electrocardiographyc LVH durin twelve years of follow-up and treatment.

PP.06.35 CARDIAC NITRIC OXIDE SYSTEM IS AFFECTED BY HYPOTHYROIDISM AND AGING

L. Rodriguez [1], F. Detomaso [2], P. Braga [3], M. Cufre Barbieri [4], P. Urrere [5], A. Moyano [6], A. Balaszczuk [7], A. Fellet [8]. *[1] School of Pharmacy and Biochemistry, Buenos Aires, ARGENTINA, [2] IQUIMEFA-CONICET, Buenos Aires, ARGENTINA, [3] University of Buenos Aires, Buenos Aires, ARGENTINA*

Objective: The aim of this study was to evaluate the involvement of nitric oxide (NO) in the hemodynamic
alterations during hemorrhagic shock in hypothyroid adult rats.

Group	EC	EH	hC	hH
NOS A (pmol.10²/g.h)	5,10±0.50	56,14±2.57*	1,47±0.21#	23,7±1.14*
NOS V (pmol.10²/g.h)	1,63±0.014	1,88±0.015	4,4±0.018#	4,47±0,05
eNOS A (UA)	0.39±0.012	3.89±0.11*	0.88±0.02#	2.42±0.29*
eNOS V (UA)	0.61±0.004	0.9±0.3*	0.564±0.003	1.281±0.11*
iNOS A (UA)	0.33±0.01	0.848±0.002*	0.573±0.005#	0.923±0.003*
iNOS V (UA)	0.61±0.001	0.85±0.17*	0.56±0.002	0.99±0.19*

Design and method: Sprague-Dawley male rats, euthyroid (E) and hypothyroid (h), 18 months of age were divided into four groups: Group C: controls; Group H: hemorrhage (withdrawal of 20% of total blood volume); Group L+C: controls + L-NAME infusion (0,5 mg/kg/h IV = 100 µl/h) and Group L+H: L-NAME infusion + hemorrhage. The hypothyroidism was induced by metimazol treatment (0,02% in the drinking water) during 28 days. Mean arterial pressure (MAP) and heart rate (HR) were recorded during 120 minutes after bleeding. The right atria (A) and the left ventricle (V) were removed in order to determine NO synthase (NOS) activity ([14]-L-citrulline method) and protein levels (western blot). The results were expressed as X±SEM, n=6/group. ANOVA analysis followed by the Tukey test *p<0.05 vs. C; # p<0.05 vs EC.

Results: In the H group, the MAP decreased about 34%, stabilizing at 90 minutes. Among hypothyroids, the fall was 48% and there was no stabilization of this parameter. L-NAME treatment only recovered MAP in euthyroid rats. The bleeding induced bradycardia followed by tachycardic response. HR reached the stabilization phase at 90 minutes in the euthyroid group (FC=392±5 bpm). The L-NAME blunted these effects in euthyroid animals. Meanwhile, NOS inhibition attenuated them over hypothyroids. The hemorrhage increased NOS activity and eNOS as well as iNOS protein levels in all groups, being lower in hypothyroids animals. In the V, the bleeding did not modify the NOS activity but increased eNOS and iNOS protein levels in all groups

Conclusions: NO system is modified by the hypothyroidism, as it lightens the hemodynamic alterations induced by the hemorrhagic shock. Thyroid hormones would differentially modulate NO production depending on the heart chamber studied.

PP.06.36 VALUE OF HIGH-FREQUENCY MID-QRS ANALYSIS COMPARED TO EXERCISE TOLERANCE TEST IN PATIENTS WITH CHEST PAIN, NONDIAGNOSTIC ECG AND HIGH PREVALENCE OF LONG-STANDING HYPERTENSION

A. Conti, A. Alesi, G. Aspesi, A. Coppa, S. Bianchi, D. Lazzeretti, S. Bigiarini, A. Becucci, F. Trausi, S. Gualtieri. *Emergency Medicine and Chest Pain Unit, Department of Critical Care Medicine and Surgery, Careggi University Hospital, Florence, ITALY*

Objective: Patients with acute chest pain (CP) and negative baseline screening for coronary artery disease (CAD) usually undergo exercise tolerance test (ETT) for risk-stratification. Analysis of ETT with high-frequency QRS components (HF-QRS) has been proposed, however the value of this novel technique has not been yet validated in patients with hypertension. The aim of this study was to compare the prognostic value of ETT to HF-QRS-analysis.

Design and method: Chest pain patients with normal ECGs, troponin, and echocardiography were enrolled, and excluded when presented QRS >=120 msec. All patients underwent maximal ETT, HF-QRS, and ETT-Echocardiography (ETT-echo). The ETT was considered positive when the ECG showed ST-segment depression >=2 mm or >=1 mm associated with CP. The ETT-echo if newer wall motion abnormalities were identified. The reduction of HF-QRS intensity >=50% of the signal recorded in two contiguous leads, at least, was considered positive.
The endpoint was the composite of coronary stenosis >=50% or acute coronary syndrome, revascularization, cardiovascular death at 3-month follow-up.

Results: Out of 175 patients considered, 142 were enrolled (mean age 58±17 years). At baseline, long-standing hypertension account for 50% of patients, dyslipidemia 29%, cigarettes smoking 24%, family history of CAD 22%, and diabetes mellitus 13%. Overall, 15 patients achieved the endpoint. At univariate analysis, hypertension (p=0.028, Hazard Ratio, HR, 3.84, Confidence Intervals, CI, 1.2-12.7), known ischaemic cardiovascular disease (p=0.015, HR, 4.0, CI, 1.3-12.0), positive HF-QRS-analysis (p=0.012, HR 4.7, CI 1.4-15.6), positive ETT (p=0.004, HR31.5, CI 3.0-326,8) and positive ETT-echo (p<0.001, HR 46.8, CI 11.3-193.7) were predictors of the endpoint. However, at multivariate analysis, only ETT-echo was predictor of the endpoint.
Interestingly, the HF-QRS-analysis was more sensitive (73% vs. 20%; p<0.01), but less specific (63% vs. 99%; p<0.001) than the ETT; when compared to ETT-echo it showed comparable sensitivity (73% vs. 80%; ps=NS) and lower specificity (63% vs 92%; p<0.001). The three techniques showed comparable negative predictive value (HF-QRS-analysis 95%, ETT 91%, and ETT-echo 98%; p=NS).

Conclusions: In patients with CP, high prevalence of hypertension, and baseline negative screening for CAD, the novel HF-QRS-analysis shows a valuable incremental prognostic value when compared with ETT.

PP.06.37 CASCADE TESTING FOR LONG QT SYNDROME IN SCOTLAND

C. Brown [1], D. O'Sullivan [2], S. Tennant [2], J. Dean [2], V. Murday [3], D. Oxnard [3], H. Hailey [2], A.C. Rankin [1], E.S. Tobias [1,3], C. Delles [1]. *[1] University of Glasgow, Glasgow, UNITED KINGDOM, [2] Nhs Grampian, UNITED KINGDOM, [3] Nhs Greater Glasgow and Clyde, Glasgow, UNITED KINGDOM*

Objective: Long QT syndrome (LQTS) has a prevalence of 1 in 2,000 – 1 in 3,000 and is characterised by QT interval prolongation on the electrocardiogram (ECG). There is marked inter- and intra-familial variability in phenotype, with symptoms ranging from loss of consciousness (syncope) to life-threatening ventricular arrhythmias and sudden death. In the general population, QT interval prolongation is associated with an increased risk of sudden death, and a prolonged QT interval is a known risk factor for ischemic heart disease in hypertensive subjects.

Design and method: We sought to evaluate cascade testing for LQTS in Scotland up to 31st May 2013. Cascade testing is a mechanism for identifying people at risk of a genetic condition by a process of family tracing. Genetic testing is offered to relatives if a disease-causing mutation has been identified in the index individual (proband). LQTS testing was established in Aberdeen in 2006 with sequencing of the 5 commonest genes (KCNQ1, KCNH2, SCN5A, KCNE1 and KCNE2). Results are classed as follows: Class 5- definite pathogenic mutation, Class 4- likely pathogenic, Class 3- variant of unknown clinical significance and Class 2- unlikely pathogenic.

Results: Genetic testing for LQTS in 541 individuals identified 116 (21.4%) LQTS mutation positive (Class 5 & 4) probands. Families of 92 (79%) of them underwent cascade testing and 426 relatives came forward for testing generating 4.6 cascade tests per family. Of the 426 cascade tests, 223 (52.3%) were mutation positive. In compari-

son with other conditions tested at the same laboratory, there were 3.3 and 2.8 cascades per family for familial hypercholesterolaemia and BRCA1 respectively. Amongst probands tested for LQTS who were mutation (Class 5 & 4) negative, 22 probands had a Class 3 variant and 57 probands had a Class 2 variant detected.

Conclusions: Cascade testing for LQTS in Scotland successfully identifies cases where a pathogenic mutation has been found in the proband. More family members are coming forward for cascade testing in LQTS in comparison with some other conditions tested by the same laboratory.

PP.06.38 MICRORNA MEDIATED TELOMERE ATTRITION LEADING TO CARDIAC HYPERTROPHY

S. Booth [1], F.Z. Marques [1], P.R. Prestes [1], P. Lewandowski [2], S.B. Harrap [3], F.J. Charchar [1]. *[1] School of Health Sciences, Federation University, VIC, Ballarat, AUSTRALIA, [2] School of Medicine, Deakin University, VIC, Geelong, AUSTRALIA, [3] Department of Physiology, University of Melbourne, VIC, Melbourne, AUSTRALIA*

Objective: Both the shortening of telomeres – the specialised DNA-protein structures that cap the ends of chromosomes – and abnormal expression of microRNAs – small, regulatory non-coding RNAs – have been associated with cardiac hypertrophy. The Hypertrophic Heart Rat (HHR) is a unique normotensive model of spontaneous polygenic ventricular hypertrophy that predisposes to cardiac failure and premature death. The aim of our study was to investigate whether there are changes in microRNA expression in the heart of the HHR that regulate telomeric genes and lead to cardiac abnormalities.

Design and method: Agilent arrays were used to measure the expression of cardiac microRNAs/mRNA in neonatal HHR in comparison to its control strain, the normal heart rat (NHR) (n=8/group) and differences were then validated by quantitative real-time PCR (qPCR). DNA was extracted from left ventricle tissue (n=16 neonates and n=21 adults) and circulating leukocytes (adults only), and relative telomere length measured by qPCR based on the Telomere to Single-copy gene (T/S) ratio method.

Results: miR-34a was the most differentially expressed microRNA in neonatal hearts, and validation by qPCR confirmed it was significantly over-expressed in both neonatal (P=0.0015) and adult (P<0.001) HHR hearts. Using miRNA prediction tools, we identified the target gene of miR-34a, Ppp1r10 (protein phosphatase 1 nuclear-targeting subunit [PNUTS]), which is known to regulate telomere length. PNUTS was down-regulated in neonatal (P=0.030) and adult (P=0.021) HHR. Telomeres were significantly longer (P=0.013) in the heart of neonatal HHR but shorter in the heart (P=0.012) and circulating leukocytes (P=0.007) of adult HHR. Both miR-34a and cardiac telomere length were correlated with heart size (P<0.05).

Conclusions: These data indicate that higher miR-34a expression leads to lower PNUTS mRNA and increased telomere attrition. Transient therapeutic suppression of miR-34a or increasing PNUTS activity could be beneficial to cardiac remodelling and function.

PP.06.39 LEFT ATRIAL VOLUME AND CARDIAC ECTOPIES IN ELDERLY ESSENTIAL HYPERTENSIVE PERSONS

D. Glukhovskoy, A. Barsukov, A. Gordienko.
Military Medical Academy, Saint-Petersburg, RUSSIA

Objective: To assess prevalence of supraventricular and ventricular arrhythmias in elderly essential hypertensive persons depending on left atrial (LA) volume, indexed by body surface area (LAVI, ml/m²).

Design and method: We have taken 189 elderly (equal to or greater than 65 yrs old) essential hypertensive persons of the total sample (364 patients). 113 subjects had normal LAVI (23,6±3,3) and 79 patients had enlarged LAVI (35,2±6,8) (p<0,001). Cutoff value of enlarged LAVI was 29 ml/m². Persons with normal and enlarged LAVI were matched for age (65,3±3,4 vs 66±4,2 yrs, p=0,8), gender (the share of men – 49 vs 59%, p=0,17), body mass index (28,5±3,1 vs 28,3±3,0 kg/m², p=0,64). The office pulse blood pressure did not differ significantly (57,5±3,4 vs 60,5±4,1 mmHg, p=0,08). Subjects with valvular and thyroid diseases did not include in the research. All patients were underwent to 24-h electrocardiogram monitoring. Data are specified as mean ± standard deviation or as percents (%).

Results: Among patients with normal and enlarged LAVI the prevalence (in %) of frequent (equal to or greater than 30 beats per any hour of monitoring) supraventricular extrasystoles, atrial fibrillation, frequent ventricular extrasystoles were equal to 13,6 and 28,1 (p=0,05); 20,4 and 36,8 (p=0,001); 9,1 and 18,4 (p=0,02) respectively.

Conclusions: Enlarged LAVI is an important marker of not only supraventricular but and ventricular arrhythmias in elderly essential hypertensive persons.

PP.06.40 THE PREVALENCE OF AORTIC REGURGITATION IN HYPERTENSIVE ALBANIAN PATIENTS

A. Banushi, V. Paparisto, E. Petrela, E. Konda, I. Refatllari, A. Goda
Cardiology Department, UHC, Nene Tereza, Tirana, ALBANIA

Objective: Association of hypertension with aortic root dilatation and aortic regurgitation (AR) is controversial. The degree to which AR is attributable to hypertension alone has been debated.
Our aim is to evaluate the prevalence of AR in hypertensive patients.

Design and method: We studied 915 patients (age 30- 75 years) with essential arterial hypertension and 159 normotensive age-matched subjects. M-mode and two echocardiographic analysis were performed to determine the aortic root diameter at the level of the sinuses of Valsalva, the chambers dimensions, wall thickness, left ventricular mass and left ventricular mass index. Color Doppler was performed to evaluate the presence and the degree AR.

Results: In the first group, 16.8% (154/915) of patients had AR, 1.75% (16/915) of them had moderate AR, whereas, 3.1% (5/159) of controls had mild AR (p<0.001). Aortic diameter at sinuses of Valsalva was 3.3± 0.44 versus 32.3± 0.36 cm (p=ns), in hypertensive versus normotensive subjects. In hypertonic patients AR was not related to sinuses of Valsalva diameter (r=0.077), but was related to aortic valve fibro-calcification (r=0.24), and left ventricular hypertrophy (r=0.28).

Conclusions: We found a higher prevalence of aortic regurgitation in hypertensive than in normotensive subjects. Careful echocardiographic evaluation is needed to prevent cardiac complications over the lifetime of hypertensive population.

PP.06.41 DEHYDRATION: NITRIC OXIDE SYSTEM AND CAVEOLINS ARE INVOLVED IN CARDIAC FUNCTION DURING AGING

P. Arza [1], V. Netti [1], F. Perosi [2], G. Cernadas [2], A. Fellet [1], A. Balaszczuk [1]
[1] Department of Physiology, Faculty of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, ARGENTINA, [2] Department of Cardiology, Aeronautical Air Force Hospital, Buenos Aires, ARGENTINA

Objective: To evaluate the effects of osmotic stress caused by controlled long-term water restriction on cardiac NO system during aging.

Design and method: Male Sprague-Dawley rats of 2 (young) and 16 months (adult) of age were divided into E1: water restriction 3 days + 1 day of hydration (1 cycle) , repeating this cycle 8 times; C1: water ad libitum (1 month). At the beginning and end of each period we determined: a) systolic blood pressure by indirect method (SBP, mmHg), b) electrocardiogram and echocardiogram: heart rate (HR); end diastolic and systolic volume (EDV; ESV), systolic volume (SV) and ejection fraction (EF). Finally, animals were sacrificed and the left ventricle (LV) was extracted to evaluate NO synthase (NOS) activity (conversion to [14C]-L-arginine to [14]-L-citrulline and NOS and cav 1 and 3 protein levels (Western Blot). Data are expressed as mean (X) ± standard error of the mean (SEM). To analyze the data we used ANOVA followed by Tukey -b test for multiple variables and Tamhane - T2 test. Significancewas 5 % probability.

Results:

	Young		Adult	
	C1	E1	C1	E1
Body weight (g)	303 ± 11	194 ± 7*	611 ± 14†	414 ± 16* †
Hematocrit (%)	47 ± 1	56 ± 1*	49 ± 1	62 ± 2*
Plasma Osmolarity (mOSM)	310 ± 2	355 ± 7*	308 ± 2	337 ± 4*
SBP (mmHg)	109 ± 1	91 ± 3*	108 ± 2	82 ± 3*
HR (lpm)	335± 6	379 ± 4*	357 ± 6	327 ± 5*†
EDV (ml)	0.11±0.01	0.09±0.01	0.26±0.02†	0.27±0.01†
ESV (ml)	0.020±0.001	0.013±0.002	0.070±0.001†	0.067±0.002†
SV (ml)	0.090±0.003	0.080±0.011	0.193±0.021†	0.220±0.015†
EF (%)	81 ± 3	82 ± 2	73 ± 4	76 ± 2

* P<0,05 vs. respective control, † P<0,05 vs. respective young rats (C1, E1)
In control adult LV animals, NOS activity was higher in comparison to the young group; however, endothelial NOS, cav-1 and cav-3 protein levels were lower in this age group. NOS activity decreased after controlled water restriction in both age groups. NOS isoforms were not affected by the dehydration. Cav-1 and 3 protein levels increased after water restriction, being this increase lower in adult animals.

Conclusions: Water restriction induced a hypovolemic state in both age groups, evidenced by the decrease in body weight and changes in biochemical parameters. Cardiac NO system and its regulatory proteins cav changes in order to preserve cardiac function and to compensate the functional alterations induced not only by the aging process but by hypovolemic state as well.

PP.06.42 FEBUXOSTAT AMELIORATES DOXORUBICIN-INDUCED CARDIOTOXICITY IN RATS

D. Arya, B. Krishnamurthy, N. Rani, S. Bharti
All India Institute of Medical Sciences, New Delhi, INDIA

Objective: Doxorubicin, a routinely used chemotherapeutic agent, has its use highly limited by the occurence of cardiotoxicity as an adverse reaction, which is a manifestation of free radical production. As a result, we evaluated an antioxidant, febuxostat, a xanthine oxidase inhibitor, in rats exposed to doxorubicin.

Design and method: Male albino Wistar rats were divided into four groups: Control (Normal saline 2.5 mg/kg/day on alternate days, a total of 6 doses; Dox (2.5 mg/kg/day on alternate days, a total of 6 doses), doxorubicin + febuxostat (10 mg/kg/day for 14 days) and doxorubicin + carvedilol (30 mg/kg/day for 14 days).

Results: Febuxostat significantly ($p<0.05$) ameliorated the deranged cardiac functions (as evidenced by decreased left ventricular end diastolic pressure and improved inotropic and lusitropic states) in doxorubicin-administered rats. It also preserved the myocardial architecture on light and electron microscopy by decreasing fibrosis. These changes were corroborated with biochemical markers, wherein febuxostat reduced thiobarbituric acid reactive substances levels and elevated glutathione (reduced form) levels and manganese superoxide dismutase activity. It also reduced cardiac injury markers (creatine kinase-MB and B-type natriuretic peptide activity) and expression of inflammatory and apoptotic proteins (TNF-alpha, nuclear factor-kappa B, Bax, Bcl-2 and caspase 3). All these changes were similar to those produced by carvedilol.

Conclusions: The antioxidant effect of febuxostat contributes to its cardioprotection against doxorubicin-induced cardiotoxicity

PP.06.43 INFLUENCE OF NITRIC OXIDE SYSTEM AND OXIDATIVE STRESS IN THE CARDIAC ALTERATIONS INDUCED BY ZINC DEFICIENCY

C. Arranz, L. Juriol, N. Gobetto, F. Mendes Garrido, G. Pineda, D. Cardelli Alcalde, F. Brunello, V. Radionovas, R. Elesgaray, A. Tomat. *Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, IQUIMIEFA-CONICET, Buenos Aires, ARGENTINA*

Objective: Moderate zinc deficiency during intrauterine and postnatal growth induces cardiovascular disorders in adult males, characterized by an increase in blood pressure levels and a decrease in wall thickness and left ventricular (LV) contractility. In turn, coronary arteries exhibited a hypertrophic remodeling associated with increased blood pressure.
To evaluate nitric oxide (NO) system and oxidative stress levels in adult male rats exposed to fetal and postnatal zinc deficiency.

Design and method: Female Wistar rats received during pregnancy up to weaning low (L:8 ppm) or control (C:30 ppm) zinc diet. After weaning, male offspring fed low (l) or control (c) zinc diet during 60 days (Cc, Ll, Lc). At day 81, we measured systolic blood pressure (SBP,mmHg,tail-cuff technique) and we evaluated in LV: basal NOS and endothelial(eNOS), neuronal(nNOS) e inducible(iNOS) isoforms activities (pmol 14C L-citrulline/g.tissue.min); eNOS protein expression (western blot; optical density eNOS/β-actin relative to Cc) and mRNA expression (RT-qPCR; eNOS/GAPDH relative to Cc), lipid peroxidation end products (TBARS, nmol/mg protein) levels, catalase(pmol/mg protein), glutathione peroxidase(GPx, µmol/min.mg.protein), superoxide dismutase(SOD, USOD/mg protein) activities and glutathione concentration(GLUT, mg/mg protein).
Values are means±SEM, n=6/group. One way ANOVA, Bonferroni post-test

Results:

	Cc	Ll	Lc
SBP	126±1	143±1*	146±2*
NOS activity	204±6	164±10*	157±11*
eNOS protein expression	1,0±0,1	0,9±0,1	1,3±0,2
eNOS mRNA expression	1,00±0,07	1,24±0,10	0,93±0,03
TBARS	0.21±0.02	0.78±0.08*	0.47±0.02*†
GLUT	1.8±0.3	0.6±0.1*	1.6±0.3
SOD	3,7±0,5	6,3±0,7*	6,4±0,4*
GPx	80±3	99±7*	92±2

*p<0.01vs Cc; †p<0.01vs Ll.
Basal NOS activity was not affected by nNOS and iNOS inhibitors, but was decreased by blocking Ca2+-calmodulin(Cc:47±2#,Ll:52±2#,Lc:49±2#,#p<0.001 vs. basal) in all groups. Catalase activity is similar in all groups.

Conclusions: Moderate zinc deficiency during fetal and postnatal life programs a lower production and bioavailability of cardiac NO, mostly, due to decreased activity of eNOS and increased levels of oxidative stress. The greater antioxidant enzymes activities would be a compensatory response to the increase in free radicals. Oxidative stress and NO impairment, jointly with other humoral, inflammatory and apoptotic mechanisms, could contribute to the cardiac disorders observed in adult males. Adequate zinc diet after weaning was unable to total avoid the cardiac alterations induced during fetal life.

PP.06.44 THE INFLUENCE OF COMBINED THERAPY WITH NEBIVOLOL AND LERCANIDIPINE ON LEFT VENTRICULAR DIASTOLIC FUNCTION AND HYPERTROPHY IN PATIENTS WITH ESSENTIAL HYPERTENSION

A. Aleksanyants [1], E. Ter-Stepanyants [2], A. Naghdalyan [2], L. Aleksanyan [2], A. Ordyan [2]. *[1] Shengavit Mc, Yerevan, ARMENIA, [2] Yerevan State Medical University, Yerevan, ARMENIA*

Objective: To assess the effectiveness of combined therapy with Nebivolol and Lercanidipine on left ventricular diastolic dysfunction and hypertrophy in patients with essential hypertension.

Design and method: This study included 44 hypertensive patients, 22 men and 22 women (mean age 55.6±8.2 years). Mean duration of hypertension was 8.1±4.2 years. Initial systolic blood pressure (mmHg) – 164.5±11.4, diastolic blood pressure (mmHg) – 95.8±8.8, heart rate (bpm) - 89,4±2,7. Left ventricular mass index (LVMI) >120 g/m2 (for men) and >100 g/m2 (for women) considered as left ventricular hypertrophy (LVH). Diastolic heart function was assessed by the following Doppler EchoCG parameters: early (E) and late (A) peak velocities, E/A ratio, isovolumic relaxation time (IVRT) and deceleration time of early peak velocity (DT).
All patients were treated with Nebivolol 5 mg plus Lercanidipine 10-20 mg daily for 8 month after one-week washout period. Doppler EchoCG parameters of diastolic function and left ventricular mass index were determined at baseline and every 2-month. Systolic and diastolic blood pressure and heart rate were measured every month.
The relationship between parameters was established by Spearman correlation analysis, $P < 0.05$ was considered statistically significant.

Results: After 8 month of the treatment LVMI was decreased from 131,5±4.3 g/m2 to 116.1±3,3 g/m2 ($p < 0.001$), E/A ratio increased from 0,84±0,22 to 1,01±0,22 ($P < 0.002$), shortened isovolumic relaxation time (IVRT) from 117±11 ms to 97±11 ms ($p < 0.001$), and decreased deceleration time (DT) from 217±22 ms to 186±16 ms ($p = 0.002$). Systolic and diastolic blood pressure was significantly reduced from 164,5±11,4 to 132,2±11,4 mmHg ($P < 0.001$) and from 95,8±8,8 to 82,6±5,8 ($P < 0.001$), heart rate from 89,4±2,7 bpm.to 71,2±5,6 bpm ($P < 0.001$).

Conclusions: These results indicate that combined therapy with Nebivolol and Lercanidipine effectively controls systolic and diastolic blood pressure, heart rate and significantly improves diastolic function in patients with essential hypertension.

PP.06.45 RESTING BLOOD PRESSURE IS LIMITING FACTOR OF MAXIMAL FUNCTIONAL AEROBIC CAPACITY IN PROFESSIONAL MALE ATHLETES

M. Zdravkovic [1], S. Mazic [2], M. Djelic [2], I. Nedeljkovic [3], M. Dekleva [4], T. Acimovic [2]. *[1] University Hospital Medical Center Bezanijska kosa, Faculty of Medicine, University of Belgrade, Belgrade, SERBIA, [2] Institute for Physiology, Faculty of Medicine, University of Belgrade, Belgrade, SERBIA, [3] Institute for Cardiovascular Diseases, Belgrade, SERBIA, [4] University Clinical Center Zvezdara, Department of Cardiology, Belgrade, SERBIA*

Objective: Hypertension as a strong determinant of cardiovascular risk has been documented among elite athletes. Even increased blood pressure (BP), but still no hypertension, could be also negative predictive factor for maximal oxygen uptake (VO2 max). The aim of the study was to evaluate the influence of the resting BP values to the maximal functional aerobic capacity of the cardiovascular system.

Design and method: A total of 585 men professional athletes from a variety of sports were examined. BP levels were divided according to the ESH/ESC guidelines in 4 groups (group I- optimal: <120/80, group II – normal: 120/80-129/84, group III – high normal: 130/85-139/89 and group IV - hypertension: >140/90 mm Hg). Maximal exercise and recovery characteristics were obtained during a graded treadmill test until exhaustion: maximal oxygen uptake (VO2 max), heart rate (HRmax) and blood pressure (TA max).

Results: The players mean age was 21,5 years (13-58), heart rate 62 ± 10 bpm, and mean BP 115/73 ± 10/8 mmHg. 462 (79,2%) athletes had optimal blood pressure, 83 (14.2%) had normal BP, while groups III and IV counted 32

(5,5%) and 6 (1%) athletes respectively. VO2 max was 52± 7 ml/min/kg, mean maximal heart rate was 187±11 bpm and mean BP was 178/54± 19/16 mm Hg. There was a statistically significant difference between the BP groups and HR max and VO2 max. Athletes with optimal BP had statistically significant higher HR compared to athletes from the group II, $p = 0.017$. Athletes with optimal rest BP had significantly higher VO2max compared to all other athletes. $p = 0.01$. Also, the strongest effect size (eta-squared = 0.06) correlation existed between rest BP and maximal systolic pressure in all groups, $p < 0.01$).
There was a significant negative linear relationship between maximal systolic blood pressure, maximal oxygen uptake and HR max, $p<0.01$.

Conclusions: Optimal BP in athletes is very important for the best maxinal functional aerobic capacity. BP elevation, even in the range of still not pathological values, is negative predictive factor for maximal oxygen uptake (VO2 max).

POSTERS' SESSION

POSTERS' SESSION PS07
ENDOTHELIUM

PP.07.01 DIAGNOSTIC SIGNIFICANCE OF ESTIMATION OF THE LEVELS OF ENDOTHELIN-1 AND NITRATES/ NITRITES IN ENDOTHELIAL DYSFUNCTION AMONG SUBJECTS WITH ARTERIAL HYPERTENSION

L. Yankouskaya, V. Snezhitskiy, S. Lyalikov.
Grodno State Medical University, Grodno, BELARUS

Objective: The most important vasoactive substances secreted by vascular enthothelium are nitric oxide (NO) and endothelin.The aim of the study was to evaluate the possibility to diagnose endothelial dysfunction (ED) in subjects with stage II arterial hypertension (AH) by the content of endothelin-1 (end-1) and nitrite/nitrate in blood serum.

Design and method: We performed a cross-sectional cohort study of 141 women with AH stage II (50,8±6,0 years). We determined the content of vasoconstrictor end-1 in blood serum (n=90) using the IBL reagent (Germany) with the help of the immunoenzymatic analyzer Sunrise (Austria). We also determined the total content of the end metabolites of NO – nitrites/nitrates (NOx) in blood serum which reflect the production of vasodilators by vascular endothelium using Griess method. We evaluated endothelium-dependent vasodilation (EDV,%) using the reactive hyperemia test by means of impedance rheography. EDV was considered to be preserved if Δ dz/dt >=12%, EDV<12% considered as ED. Statistical analysis was performed with the help of «STATISTICS 10.0». Significance of the level of end-1 and NOx for diagnosis of ED was assessed by means of ROC-analysis.

Results: Patients were divided into two groups: group 1- without ED, group 2- with ED. EDV in group 1 was 34[23;53]%, in group 2 -5[-18; 5]%. In group 2 the level of end-1 was higher (0.57±0.18 pg/ml,p=0.032), and NOx lower (15.2[11.1; 29.9] µmol/l,p=0.0005), than in group 1 (0.49±0.21 pg/ml and 22.8[16.9;33.0] µmol/l, respectively). In group 1 there was a correlation relationship between EDV and end-1 (R=-0.26; p=0.044), in group 2 - between EDV and NOx (R=0.36;p=0.011). The optimal cut-off point which allowed with 76% sensitivity predict ED corresponded to the level of end-1 >=0,53 pg/ml, specificity being 62%. The optimal cut-off point which allowed with 69% sensitivity predict ED corresponded to the level of NOx <=16,5 µmol/l, specificity being 66%.

Conclusions: The level of end-1>=0.53 pg/ml and NOx<=16.5 µmol/l with high sensitivity and specificity allows to diagnose presence/absence of ED in females with stage II AH.

PP.07.02 RELATIONSHIP BETWEEN VITAMIN D, PARATHYROID HORMONE AND ENDOTHELIAL FUNCTION IN FEMALES WITH ARTERIAL HYPERTENSION

L. Yankouskaya, V. Snezhitskiy.
Grodno State Medical University, Grodno, BELARUS

Objective: The aim of the study was to assess the effect of vitamin D and parathyroid hormone (PTH) on the values of systolic and diastolic blood pressure (SBP, DBP) as well as endothelial function.

Design and method: We performed a cross-sectional cohort study of 141 women (50,8±6,0 years) with arterial hypertension (AH) and 25 healthy women (46,8±6,5 years). We determined the content of vitamin D-total (25(OH)D2+25(OH)D3), PTH in blood serum using the DRG reagent (USA) and endothelin-1 (end-1) using the IBL reagent (Germany) with the help of immunoenzymatic analyzer Sunrise (Austria). Plasma nitrite/nitrate level (NOx) was determined using Griess method. We evaluated endothelium-dependent vasodilation (EDV) using the reactive hyperemia test by means of impedance rheography. EDV was considered to be preserved if Δ dz|dt exceeded 12%, if Δ dz|dt was less than 12% the condition was considered as endothelial dysfunction (ED).

Results: EDV was higher (p=0.05) in control group 23.9±14.7%, than in group with AH 15.3±28.0%. The levels of end-1 and NOx did not differ between the group with AH (0.52(0.38;0.59)pg|ml and 17.0(11.5;29.1)µmol|l) and the control group (0.53±0.07pg|ml and 18.2(13.2;24.4)µmol|l). The level of 25(OH)D-total also did not differ among the groups (23.8(16.3;33.1) and 24.87±9.99 ng|ml). The level of PTH was higher in control group (43.93±15.79pg|ml). In the group with AH there was a correlation between SBP and 25(OH)D-total (R=-0.23;p=0.034), SBP and PTH (R=0.28;0.003), PTH and NOx (R=-0.24;p=0.03). All the subjects were divided into two groups: group 1–without ED, group 2–with ED. In group-2 the level of end-1was higher (p=0.032), and NOx lower (p=0.0005), than in group-1. In group-2 correlation between PTH and NOx increased (R=-0.48;p=0.003). In group-1 the contribution of the cluster endothelial functions to the values of SBP and DBP was minimal. In group-2 relationship between SBP and NOx (R=-0,55), SBP and EDV (R=-0,47), as well as between DBP and NOx (R=-0,45), DBP and EDV (R=-0,31) was more pronounced.

Conclusions: The values of SBP are associated with the level of 25(OH)D and PTH. Endothelial function is regulated by 25(OH)D and PTH, and plays an important role in maintaining the values of SBP and DBP when ED develops.

PP.07.03 L-ARGININE AND ARGINASE PRODUCTS POTENTIATE CONTRACTIONS TO DEXMEDETOMIDINE IN THE RAT AORTA WITH ENDOTHELIUM IN THE PRESENCE OF N Ω-NITRO-L-ARGININE METHYL ESTER

E.S.W. Wong [1,3], R.Y.K. Man [1], P.M. Vanhoutte [1], K.F.J. Ng [1,2]. *[1] The University of Hong Kong, Department of Pharmacology and Pharmacy, Hong Kong, HONG KONG, [2] The University of Hong Kong, Department of Anaesthesiology, Hong Kong, HONG KONG, [3] The Open University of Hong Kong, School of Science and Technology, Hong Kong, HONG KONG*

Objective: Dexmedetomidine is an anesthetic agent which can cause relaxation [by releasing endothelium-derived nitric oxide (NO)] or contraction (by activating α1 and α2-adrenoceptors) of isolated arteries. L-arginine is the common substrate for nitric oxide synthase (NOS) and arginase I and II, and thus can be converted to either NO or arginase products (urea and ornithine). The present study investigated whether or not L-arginine or the arginase products can augment the endothelium-dependent contractions to dexmedetomidine.

Design and method: Organ chamber studies:
Thoracic aortae with endothelium were isolated from male ten-weeks-old Sprague Dawley rats and suspended in organ chambers for isometric tension recording. Cumulative concentrations of dexmedetomidine were added to quiescent aortic rings, incubated with Nω-nitro-L-arginine methyl ester (L-NAME, NOS inhibitor), L-arginine, urea or ornithine for 40 minutes.
Immunofluorescent staining:
Frozen sections of rat aortae were incubated with anti-von Willebrand factor antibody (1:50) and anti-arginase I antibody (1:50) or anti-arginase II antibody (1:50) at 4 degrees Celsius overnight, followed by 37 degrees Celsius for one hour. Then, the sections were washed and incubated with corresponding secondary antibodies (1:50) for two hours in the dark. Antifade reagent with DAPI was then added. The sections were examined under a fluorescence microscope.

Results: Dexmedetomidine caused concentration-dependent contractions in the presence of L-NAME [EMax (% of 60 m MKCl): 48.19±5.48, logEC50: -6.61±0.18] and the maximal contraction was potentiated significantly by L-arginine [EMax: 81.76±4.42 (P<0.05), logEC50: -6.68±0.09], urea [EMax: 96.31±4.72 (P<0.05), logEC50: -6.91±0.09] or ornithine [EMax: 94.68±3.88 (P<0.05), logEC50: -6.91±0.07]. These potentiations were reversed by the arginase inhibitors (S)-(2-boronoethyl)-L-cysteine (BEC) and N-hydroxy-L-arginine (L-NOHA) and were absent in preparations without endothelium. The potentiations by urea and ornithine were reversed by the addition of L-arginine. Fluorescent staining of arginase I and II confirmed the presence of the two isoforms of arginase in rat aortic endothelial cells.

Conclusions: Both urea or ornithine, downstream products of the conversion of L-arginine by arginase, potentiate contractions to dexmedetomidine in rat aortae with endothelium.

PP.07.04 THE ROLE OF INTRAUTERINE CHRONIC HYPOXIA ON VASCULAR ENDOTHELIAL FUNCTION AND NOS EXPRESSION IN RATS OFFSPRING

Z. Huang, Z. Wang. *Cardiology Department, 2nd Affiliated Hospital of Fujian Medical University, Quanzhou, CHINA*

Objective: To investigate the effects of fetal intrauterine chromic hypoxia on the vascular endothelial function and the expression of NOS in the aorta from adult offspring rats.

Design and method: Pregnant Sprague-Dawley rats were subjected to hypoxia for 2 hours in low pressure cabin with an oxygen concentration of 10%±1% from 7 to 21 days gestation. Endothelial dependent diastolic function and the expression of iNOS and eNOS in the aorta were determined.

Results: The endothelial dependent diastolic function was 45.1±14.4% in the intrauterine hypoxia group, and 82.7±10.6% in the control group. There was significant difference in it between these two groups (t=5.14,P<0.001). Compared with the control, iNOS was up-regulated predominantly in intrauterine hypoxia group at both mRNA level and protein level. In contrast, the expression of eNOS was prominently down-regulated in intrauterine hypoxia group.

Conclusions: Intrauterine chromic hypoxia can induce impaired vascular endothelium function in adult offspring rats. This efficacy might be mediated by abnormal expression of iNOS and eNOS in the blood vessels.

PP.07.05 ENDOTHELIAL NITRIC OXIDE PRODUCTION WEAKENS ARTERIAL CONSTRICTOR RESPONSES IN MOST OF ORGANS DURING EARLY POSTNATAL DEVELOPMENT IN RATS

S. Sofronova [1], A.A. Borzykh [2], O.S. Tarasova [1, 2]
[1] Lomonosov Moscow State University - Department of Human and Animal Physiology, Moscow, RUSSIA, [2] Institute for Biomedical Problems, RAS - Laboratory of Excercise Physiology, Moscow, RUSSIA

Objective: During maturation the vascular system undergoes structural and functional alterations. We showed recently that saphenous arteries of young (10-12 day old) demonstrate increased eNOS expression and a tonic nitric oxide (NO) production which contribute to lower contractile responses compared to adult rats arteries (Gaynullina et al. Cardiovasc Res 2013, 99:612-21). Here we tested the hypothesis that vasorelaxing NO influence is present not only in cutaneous circulation but also in other organs of young rats.

Design and method: The segments of saphenous, intrarenal, small mesenteric and sural arteries were isolated from young (2 wk old) and adult (10-12 wk old) rats and mounted in isometric myograph. Anticontractile effect of NO was evaluated by increases of arterial spontaneous tone and the response to methoxamine (alpha1-adrenoceptor agonist) in the presence of NOS inhibitor L-NNA vs. its inactive analogue D-NNA. In addition, we estimated eNOS and Arginase-2 mRNA expression levels in arterial preparations by qPCR, nitrite/nitrate serum levels by Griess reaction and arterial pressure (AP) levels in conscious state by intra-carotid artery catheters.

Results: In all arteries studied except renal ones, L-NNA induced tonic contraction and prominently increased the contractile response to methoxomine. By 10-12 weeks, the effect of L-NNA was very small in mesenteric arteries and disappeared in sural and saphenous arteries. Although eNOS mRNA expression levels did not differ in arteries of 2-wk old and adult rats, Arginase-2 mRNA expression level was significantly lower in young rats compared to adults. Serum level of NO metabolites was 1.5-fold higher in young than in adult rats. Along with that, mean AP levels were more than twice lower in young rats (50.9±9.0 mmHg) as compared to adults (114.9±3.4 mmHg).

Conclusions: In young rats tonic NO production by the endothelium weakens contractile responses of arteries supplying skin, small intestine and skeletal muscles. Since these organs receive a high proportion of the cardiac output, influence of NO may contribute to lowering AP level in immature circulatory system. Insufficiency of endothelial function early after birth may be the reason of cardiovascular pathologies in adulthood.

PP.07.06 PREDIABETES IS ASSOCIATED WITH EARLY CHANGES IN MICROCIRCULATION

V. Shyshko [1], T. Mokhort [1], E. Konstantinova [2], N. Tsapaeva [3].
[1] Belarusian State Medical University, Endocrinology Department, Minsk, BELARUS, [2] Belarusian Republic Center of Cardiology, Department of Chronic Heart Failure, Minsk, BELARUS, [3] Belarusian State Medical University, Department of Inner Disease 3, Minsk, BELARUS

Objective: Microangiopathy in patients with type 2 diabetes (T2D) results from previous microcirculation abnormalities (e.g. increased permeability, disturbance of intracapillary pressure and blood flow). Hyperglycemia as well as hesitance of glucose level in patients with prediabetes (impaired glucose tolerance and impaired fasting glucose) have negative impact on microvessel status.

Design and method: We included 131 patients with average age 49,03 ± 8,76 years old. Patients were divided into 2 groups: group 1 – 37 patients with prediabetes, group 2 – 35 patients with type 2 diabetes (with duration of disease no longer as 5 years and treated with oral blood glucose lowering drug) and group 3 – 59 almost healthy person. Microcirculation was measured by computer based conjunctival biomicroscopy (Malaja et al.), results were evaluated by the set of criteria for quantitative evaluation of conjunctival microcirculation: FC (number of active capillary tubes), AVA (arteriovenous anastomosis), Mean (vascular tortuosity), Sl (sludge), Mtr (microthrombosis). Severity of each criteria was scored and more sever changes had higher degree.

Results: Microcirculation abnormalities were revealed in patients with prediabetes: we registered statistically significant decrease of active capillary tubes (FC) (3,0[2,0;3,0] vs 2,0[2,0;3,0] in control group) (p1-3<0,025), increased number of AVA (2,0 [2,0; 4,0] vs 2,0 [2,0; 2,0] in control group) (p1-3<0,025) and Mtr (1,0[1,0;2,0] vs 0,0[0,0;1,0] in control group) (p1-3<0,001). Hence in patients with prediabetes we observed hypoperfusion and microthrombosis that predispose vascular wall to atherosclerosis.
We registered more significant changes in patients with T2D compared to patients with prediabetes and control group. Patients with T2D had more significant Mean (1,0[1,0;2,0]) compared to group 1 and 3 (1,0[1,0;1,0]) (p1-2 <0,05 and p2-3< 0,001 correspondingly), erythrocyte properties are also changed that is presented in sludge formation (2,0[2,0;4,0] vs 2,0[2,0;2,0] in groups 1,3) (p1-2 <0,05, p2-3<0,001 correspondingly).

Conclusions: Analysis of microcirculation demonstrate presence of changes in microvessel system during early disturbance of glucose metabolism (that is in prediabetes). T2D is associated with more significant changes in microcirculation. Damage of microvessel is one of the factors that leads to endothelial dysfunction and atherosclerosis.

PP.07.07 IMPACT OF TAI CHI EXERCISE ON THE ARTERIAL STIFFNESS ACCORDING TO DURATION IN MIDDLE-AGED FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS

B.K. Kim [1], S.J. Shim [1], J.H. Shin [2], S. Bang [3], J. Shin [2], H. Lee [3], S.G. Kim [2], B.H. Lee [4]. *[1] Cardiology, Department of Internal Medicine, SungAe General Hospital, Kwandong University College of Medicine, Seoul, SOUTH KOREA, [2] Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, SOUTH KOREA, [3] Division of Rheumatology, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, SOUTH KOREA, [4] Division of Cardiology, Department of Internal Medicine, Songdo Hospital, Seoul, SOUTH KOREA*

Objective: Rheumatoid arthritis (RA) is associated with increased risk of cardiovascular disease, and levels of early preclinical markers of atherosclerosis, such as those that reflect increased arterial stiffness, are commonly found to be higher in RA patients than healthy individuals. The aim of this study was to examine Tai-Chi exercise on arterial stiffness in middle-aged female patients with RA.

Design and method: Twenty-nine female patients aged 55-71 with RA who had been practicing Tai Chi for arthritis exercise program for 3 months were recruited from a regional hospital in Korea. We divided exercise group according to the duration of RA. Assessment of arterial stiffness was performed by using brachial-ankle pulse wave velocity (baPWV).

Results: Mann-Whitney test showed no significant difference of baPWV according to disease duration (baseline; 1691±349, p=0.080; 3 months later; 1603±291: p=0.102) After 12 weeks of Tai Chi exercise, however, we found that baPWV of the longer duration of RA patients (> 10 years) decreased from 1847±415 to 1712±349 (Wilcoxon signed rank test, p=0.013), without significant decrease in blood pressure.

Conclusions: This study shows that practicing Tai Chi exercise can improve the arterial stiffness of patients with RA. Moreover, Tai Chi could

be an attractive form of exercise for the longer duration of RA patients. Large-sized randomized clinical trials examining the effects of Tai Chi on cardiovascular outcomes are required.

PP.07.08 THE BENEFICIAL EFFECTS OF TAI CHI ON ENDOTHELIAL FUNCTION IN MIDDLE-AGED WOMEN WITH RHEUMATOID ARTHRITIS

J. Shin [1], S. Bang [2], J. Shin [1], H. Lee [2], S.G. Kim [1], B.H. Lee [3]
[1] Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, SOUTH KOREA, [2] Division of Rheumatology, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, SOUTH KOREA, [3] Division of Cardiology, Department of Internal Medicine, Songdo Hospital, Seoul, SOUTH KOREA

Objective: Rheumatoid arthritis (RA) is associated with increased risk of cardiovascular disease, and levels of early preclinical markers of atherosclerosis, such as those that reflect increased arterial stiffness, are commonly found to be higher in RA patients than healthy individuals. We investigated the effects of Tai-Chi exercise on endothelial function and arterial stiffness in middle-aged women with rheumatoid arthritis.

Design and method: Fifty-six age-matched, body mass index (BMI)-matched female patients aged 55-71 with rheumatoid arthritis were allocated to either an exercise group, practicing Tai Chi exercise program for 3 months, or controls receiving only information about the benefits of exercise. Participants were assessed for arterial stiffness and endothelial function by using brachial-ankle pulse wave velocity (baPWV) and flow-mediated dilatation (FMD). Data were collected at baseline and at the end of the intervention (3 months).

Results: At baseline, demographic, disease-related characteristics as well as baPWV and FMD were similar between Tai Chi exercise and control groups ($p>0.05$). After 3 months of Tai Chi exercise, Mann-Whitney test revealed a significant improvement in FMD in the Tai Chi exercise compared to control group ($p=0.016$), without significant decrease in blood pressure and lipid profile. However, baPWV decreased in the Tai Chi exercise compared to control group, but no significant improvement ($p=0.078$).

Conclusions: This study shows that practicing Tai Chi exercise can improve the endothelial dysfunction of middle-aged women with rheumatoid arthritis. Therefore, Tai Chi could be an attractive form of exercise for elderly rheumatoid arthritis patients. More large-sized case-control or randomized clinical trials examining the effects of Tai Chi on cardiovascular outcomes are required.

PP.07.09 DYSFUNCTION OF TRPV4-SKCA SIGNALING PATHWAY UNDERPINS IMPAIRED EDHF-MEDIATED RESPONSE IN MESENTERIC ARTERIES OF STROKE-PRONE SPONTANEOUSLY HYPERTENSIVE RATS

T. Seki, K. Goto, K. Kiyohara, Y. Kansui, N. Murakami, Y. Haga, T. Ohtsubo, K. Matsumura, T. Kitazono. *Department of Medicine and Clinical Science, Graduate School of Medicine Sciences, Kyushu University, Fukuoka, JAPAN*

Objective: Endothelium-derived hyperpolarizing factor (EDHF)-mediated responses are impaired in hypertension; however, the underlying mechanisms have not been determined yet. The activation of small- and intermediate- conductance of Ca2+-activated K+ channels (SKCa and IKCa) underpins EDHF-mediated responses. Recently, it has recently been reported that Ca2+ influx through endothelial transient receptor potential vanilloid type 4 (TRPV4) channels is a prerequisite for the activation of SKCa and IKCa in arterial endothelial cells. The aim of the present study was to investigate whether impairment of EDHF-mediated responses in hypertension is attributable to the dysfunction of TRPV4 and/or KCa channels.

Design and method: In the presence of phenylephrine, membrane potentials and contractile responses were recorded from the isolated superior mesenteric arteries of 20-week-old stroke-prone spontaneously hypertensive rats (SHRSP) and age-matched Wistar-Kyoto rats (WKY). Experiments were performed in the presence of indomethacin and NG-nitro-L-arginine to inhibit prostaglandins and nitric oxide, respectively.

Results: In mesenteric arteries of WKY, acetylcholine (ACh)-induced, EDHF-mediated responses were reduced by a combination of KCa channel blockers (apamin plus TRAM-34), or by blockade of TRPV4 with selective antagonist RN-1734. In mesenteric arteries of SHRSP, ACh-induced, EDHF-mediated hyperpolarization and relaxation were significantly impaired compared with WKY (hyperpolarization to 10-5 mol/L ACh: SHRSP -6±2 vs. WKY -20±2 mV, n=6-7, $P<0.05$). GSK1016790A, a selective TRPV4 channel agonist, evoked robust hyperpolarization and relaxation in arteries of WKY. In contrast, in arteries of SHRSP, GSK1016790A-evoked hyperpolarization was small and relaxation was absent (hyperpolarization to 10-8 mol/L GSK1016790A: SHRSP -1±1 vs. WKY -12±2 mV, n=5, $P<0.05$). Hyperpolarization and relaxation to CyPPA, a selective SKCa channel agonist, were significantly decreased in arteries of SHRSP compared to WKY. Hyperpolarization and relaxation to 1-EBIO, a selective IKCa channel agonist, did not differ between the two strains.

Conclusions: These findings suggest that TRPV4 and to some extent SKCa channels functions are compromised, leading to impaired EDHF-mediated responses in mesenteric arteries of SHRSP.

PP.07.10 ENDOTHELIAL FUNCTION AND PULSE WAVE VELOCITY IN PATIENTS WITH HYPERTENSION AFTER STROKE

T. Pronko, P. Masevich. *Grodno State Medical University, Grodno, BELARUS*

Objective: The aim of the study is assessment of endothelial function and arterial stiffness in patients with arterial hypertension with and without stroke.

Design and method: Study population includes 61 patients with arterial hypertension. Patients were divided into 2 groups depending of presents of stroke history. Group 1 includes 37 patients (7F/30 M, 47-62 years old, duration of hypertension 7.9±5.5 years) with arterial hypertension and stroke in history. Group 2 includes 24 patients (10F/14M, 30-63 years old, duration of hypertension 8.1±4.9 years) with arterial hypertension without stroke. Control group includes 47 healthy volunteers (14F/33M, 30-52 years old). Endothelial function was measured by impedance rheography. The forearm blood flow (FBF) was measured during reactive hyperemia to test endothelium-dependent vasodilatation. FBF was considered to be preserved if it exceeded 12%, less than 12% considered as endothelial dysfunction. Carotid femoral pulse wave velocity (PWV) was measured noninvasively.

Results: PWV in patients group 1 was higher to compare to group 2 and controls respectively (15.80±0.80 m/s; 9.33±1.26 m/s, $p<0.01$; 5.89±0.43 m/s, $p<0,0001$). FBF was smaller in patients group 1 to compare to group 2 and controls respectively (-8.21±2.71%; 6.11±2.51%, $p<0.01$; 21.84±1.71, $p<0.001$). Patients of group 1 have paradoxical reaction on reactive hyperemia as vasospasm in 75.7% cases, patients of group 2 – in 33.3% cases, controls have not paradoxical reaction on reactive hyperemia.
FBF negatively correlated with age ($r= - 0.37$, $p<0.05$) and negatively correlated with plasma cholesterol level ($r= - 0.36$, $p<0.05$) in patients of group 1.

Conclusions: Thus, patients with hypertension have increased PWV and signs of endothelial dysfunction. Quantitative assessment of endothelial dysfunction and PWV can serve not only as a diagnostic criterion, but also a dynamics of the target organ in the treatment of hypertensive patients. PWV and FBF measurements allow maximum early to identify additional risk group of hypertensive patients with minimal time and without the use of costly invasive techniques. Patients after stroke have significant increase in PWV and reduced FBF.
Such patients need correction of medicinal therapy based on the identified changes.

PP.07.11 THE EFFECT OF CAROTENOIDS AND FLAVONES ON ENDOTHELIAL FUNCTION

E. Paran [1], R. Chamias [1], L. Volvich [1], T. Wolak [2]. *[1] Faculty of Heaeh Sciences Ben-Gurion University, Beer-Sheva, ISRAEL, [2] Soroka University Medical Center, Ben-Gurion University, Beer-Sheva, ISRAEL*

Objective: Carotenoids and flavones are both have been described as powerful anti-oxidant natural substances. In previous studies we had demonstrated their blood pressure lowering effect. In the current study we aimed to evaluate the possible synergistic activity of these substances as anti-oxidant and anti inflammatory mediators on endothelial cells.

Design and method: Endothelial cells (EA.hy926) were pre-incubated with vehicle, lycopen, dissolved chocolate, epicatechin solution, combination of lycopen with chocolate and combination of lycopen with epicatechin solution for 18-24h. with or without induction with TNF-α for 6h. The activated cells were examined for protein abundance of: eNOs, adhesion molecules ICAM-1, VCAM-1 and osteopontin (OPN).

Results: There was a significant augmentation of NOx production after pre incubation with each substance separately. Moreover, the combination of lycopen with either chocolate or epicatechin resulted in synergistic effect. Lycopen with chocolate 8.1± 5.1 (OD) and lycopen with epicatechin 6.9±2.3 (OD), versus control 1.4±1.2 (OD) and lycopen 2.3±0.9 (OD) respectively ($p<0.005$). Pre incubation with lycopen, chocolate or

epicatechin didn't have significantly effect on the activation of VCAM-1 and ICAM-1by TNF-α. However, the combination of either lycopen and chocolate or lycopen with epicatechin inhibited significantly the expression of both VCAM-1 and ICAM-1induced by TNF-α (25.5±2.6 and 12.5±2.1 versus 46.6±11.6; 31.3±15.3 and 19.0±5.3 versus 45.3± 11.9 respectively p<0.001). Regarding the expression of eNOs, both lycopen, chocolate and epicatechin increased significantly the expression of eNOs. However, the combination of these sustenance didn't reach synergistic effect.

Conclusions: In the current study we demonstrated the superiority of the combination carotenoids and flavonoids compared to each substance alone, as oxidative stress and inflammation inhibitor.

PP.07.12 A NEW MARKER OF PLATELET ACTIVATION, SCUBE1, IS ELEVATED IN HYPERTENSIVE PATIENTS

G. Ozkan [1], S. Ulusoy [1], A. Mentese [2], S. Karahan [2], M. Cansiz [1]. *[1] Karadeniz Technical University School of Medicine Department of Nephrology, Trabzon, TURKEY, [2] Karadeniz Technical University School of Medicine Department of Biochemistry, Trabzon, TURKEY*

Objective: Hypertension is associated with an increase in platelet activation and endothelial dysfunction and leads to a tendency to cardiovascular events (CVEs). Signal peptide-CUB-EGF domain-containing protein 1 (SCUBE1) is a novel platelet activation marker. There are currently no studies showing the level of SCUBE1 in hypertensive patients. The purpose of this study was to determine the level of SCUBE1 in this patient group and to investigate the parameters affecting that level.

Table 1. A comparison of the demographic and biochemical parameters of the Hypertensive and Control group

	Hypertensive group (n:45) mean±sd or median (min-max)	Control group (n:21) mean±sd or median (min-max)	P values
Age	42.2±12.4	40.8±8.4	NS
Gender (F/M)	22/23	11/10	NS
BMI	28.0±4.2	26.6±3.9	NS
SBP(mmHg)	149.3±5.2	103.8±5.8	P<0.001
DBP(mmHg)	91.3±4.1	63.8±4.9	P<0.001
Glucose (mg/dL)	88.5±5.4	90.3±6.5	NS
Potassium (mmol/L)	4.5±0.4	4.5±0.4	NS
BUN (mg/dL)	12.0 (9-19)	12.0 (6-26)	NS
Creatinine (mg/dL)	0.7 (0.5-1.1)	0.7 (0.5-1.2)	NS
Uric acid (mg/dL)	4.7±1.0	4.0±1.1	P<0.05
T. chol (mg/dL)	102.0(41-281)	121.0(41-410)	P<0.05
Triglyceride (mg/dL)	163.7±100.2	111.4±60.3	P<0.05
HDL (mg/dL)	45.3±11.1	46.5±11.6	NS
LDL (mg/dL)	131.2±43.5	103.4±27.3	P<0.05
hsCRP (mg/dL)	0.3 (0-0.8)	0.3 (0-2.0)	NS
Hemoglobin(g/dL)	13.4±1.0	13.1±1.0	NS
Platelet (x10³/μL)	247.4±54.0	253.9±52.5	NS
PT(sn)	13.8±0.9	13.6±0.7	NS
aPTT(sn)	29.8±2.6	29.9±2.7	NS
Fibrinogen(mg/dL)	339.9±73.6	326.0±66.4	NS
D dimer (ng/mL)	0.7±0.2	0.6±0.3	NS

Data are presented as arithmetic mean ± standard deviation. Statistical significance was set at P<0.05.

Abbreviations: BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; BUN: Blood urea nitrogen; T. chol.: total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; High sensitive C-reactive protein (HsCRP), PT: prothrombin time, aPTT: activated partial thromboplastin time

Design and method: Forty-five newly diagnosed, untreated stage 1 hypertensive patients and 21 healthy individuals were included. Blood specimens were collected in order to determine SCUBE1, sCD40L, PT, PTT, fibrinogen, D dimer, hemogram, lipid parameters, BUN, creatinine and uric acid levels. The relation between SCUBE1 level and demographic data and biochemical parameters was then investigated.

Results: Hypertensive group SCUBE1 and sCD40L levels obtained from plasma specimens were significantly higher than those of the control group (p<0.001, P<0.05, respectively). Hypertensive group blood pressure (BP) values, uric acid, LDL, total cholesterol and triglyceride levels were also statistically higher than the control group. Parameters affecting SCUBE1 levels were systolic and diastolic BP, sCD40L, lipid parameters and uric acid levels.

Conclusions: We show, elevated levels of SCUBE1, a novel platelet activation marker, in primary hypertensive patients. We think that, when supported by further clinical studies, this newly described marker may be useful in the monitoring of CVEs in this patient group, in which platelet activation is known to be associated with such events.

PP.07.13 DOSE- AND TIME-DEPENDENT ACTIONS OF ENDOGENOUS CARDIOTONIC STEROIDS ON TRANSCRIPTOME OF HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS: EVIDENCE FOR [NA+]I/[K+] I-MEDIATED EXCITATION-TRANS

S. Orlov [1], O. Akimova [1], S. Koltsova [1], O. Lopina [1], J. Tremblay [2], P. Hamet [2]. *[1] Lomonosov Moscow State University, Moscow, RUSSIA, [2] Centre Hospitalier de l'Universite de Montreal, Montreal, CANADA*

Objective: Ouabain and marinobufagenin (MBG) are known as major endogenous cardiotonic steroids (ECTS) involved in the pathogenesis of volume-expanded disorders, including hypertension, via its interaction with endothelial, vascular and neurional cells. In spite of numerous effords, the role of Na+i/K+i-mediated and -independent signaling in cellular responses triggered by ECTS remains a unknown. This study examined the relative contribution of these signaling pathways in transcriptomic changes triggered by ouabain and MBG in human umbilical vein endothelial cells (HUVEC).

Design and method: HUVEC were incubated for 6 or 24 hr in the presence of 3, 30 and 100 nM of ouabain or MBG. Intracellular K+ and Na+ content was measured as the steady-state distribution of 86Rb, and 22Na, respectively. Total RNA was extracted and processed with a reverse transcription generating sense-strand cDNA as final product. cDNA was fragmented and labeled by Affymetrix GeneChip® kit.

Results: Six hr exposure to 30 nM ouabain did not significantly affected intracellular Na+ and K+ content whereas at concentrations of 100 nM ouabain increased the [Na+]i/[K+]i ratio by 10-fold. In contrast to 6 hr incubation, 24-hr exposure to 30 nM ouabain increased the [Na+]i/[K+]i ratio by 15-fold whereas 3 nM ouabain or MBG did not affect this parameter. In HUVEC treated with 100 nM ouabain for 6 hr or with 30 nM for 24 hrs, the total numbers of transcripts whose expression was changed by more than 1.2-fold (p<0.05) were 258 and 2185, respectively. In both cases, the list of transcripts whose expression was increased by more than 2-fold was abundant with immediate response genes such as EGR1, FOS, EGR3, JUNB, ATP3 as well as with genes encoding intermediates of cytokine signalling and prostaglandin-endoperoxide synthase PTGS2. We did not observe any transcriptomic changes in 6 hrs incubation with 30 nM as well as 24 hrs incubation with 3 nM ouabain or MBG.

Conclusions: ECTS affects transcriptome of endothelial cells via [Na+]i/[K+] i-mediated signaling pathway. The role of [Na+]i/[K+]i-independent signaling in altered functions of ECTS-treated cells should be examined further.

PP.07.14 HEART RATE VARIABILITY AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH ARTERIAL HYPERTENSION AND CORONARY ARTERY DISEASE

N. Musikhina, T. Petelina, E. Mahneva, L. Gapon
Tyumen Cardiology Center, Tyumen, RUSSIA

Objective: To study the features of heart rate variability and endothelial dysfunction in patients with arterial hypertension and coronary artery disease.

Design and method: 121 patients aged 40-70 years were examined with the aim to study the features of heart rate variability and endothelial dysfunction in patients with arterial hypertension and coronary artery disease. 18 patients were in the control group without arterial hypertension and coronary artery disease, 56 patients were in the group with arterial hypertension, 47 patients were in the group with arterial hypertension combined with coronary artery disease. For arterial pressure study and heart rate variability study the cardio monitors «Kardiotehnika-4000» («Inkart» company, Saint Petersburg) were used. Endothelial function status was assessed using sample with reactive hyperemia and sample with nitroglycerine.

Results: It was established that an increased activity of the sympathetic nervous system (SNS) influences on endothelial dysfunction (ED) formation in patients with arterial hypertension (though LF), in patients with arterial hypertension combined with coronary artery disease (through LF and VLF). Patients with arterial hypertension combined with coronary artery disease differed from patients with arterial hypertension by the presence of more evident sympatho-parasympathetic imbalance (LF/HF > 1) as compared with the reducing of all BPC indices (SDAN, SDNN, r-MSSD, HF, LF, VLF).

Conclusions: The negative influence of such factors as male sex and elderly age to endothelial dysfunction in patients with arterial hypertension combined with coronary artery disease was determined.

PP.07.15 GENDER DIFFERECES OF STABLE NITRIC OXIDE METABOLITES LEVELS IN ESSENTIAL HYPERTENSION

V. Podzolkov, A. Bragina, N. Murashko.
Sechenov First Moscow State Medical Institute, Moscow, RUSSIA

Objective: To investigate gender differences of stable nitric oxide metabolites levels (NOx) in patients with essential hypertension (EH).

Design and method: We examined 124 untreated patients (45 men and 79 women) with EH (mean age 51.4±6.5 years, mean EH duration 8.5±7.6 years) and 25 healthy volunteers (10 men and 15 women) with comparable age (47.2±7.8years). Plasma NOx levels were measured by spectrophotometry. Results were processed with Statistica 6.0 software.

Results: Results were analyzed in accordance to EH grades and age: <40, 40-59 and >=60 years. NOx levels were significantly higher in hypertensives (43.2±21.0 μmol/l) compare to controls (28.3±9.6 μmol/l) (p<0,05). Males with EH had higher NOx concentration (49.5±19.1 μmol/l) than females (42.1±22.1 μmol/l) (p<0,05). Aging was related to significant increase in NOx concentration in males with EH (37.3±9.3 in persons <40 years old, 42.5±18.7 in 40-59 years, and 62.5±30.0μ mol/l in >=60 years, p<0,05), and had U-shape curve relation in females with EH (27.6±2.6, 44.8±23.7, and 31.9±8.4μ mol/l, relatively p<0,05). In male hypertensives the highest NOx level was at grade 1, lower – at the grade 2, and the lowest – at the grade 3 EH (53.9±26.2; 44.5±17.5, and 43.4±23.9 μmol/l, accordingly) (p<0,05). Whereas females with EH didn't have significant differences of NOx levels in accordance to EH grade: 42.6±2.2, 43.9±25.3, and 40.2±20.8 μmol/l relatively (p<0,05).

Conclusions: Hypertensives demonstrate more prominent endothelial dysfunction in males related to aging and EH severity.

PP.07.16 ENDOTHELIAL DYSFUNCTION AND SALT SENSITIVITY IN SUBJECTS WITH NORMAL BLOOD PRESSURE

F. Margulis, R. Sabbatiello, C. Castro, S. Ramallo, R. Schiavelli.
Hospital General de Agudos Cosme Argerich, Buenos Aires, ARGENTINA

Objective: The aim of this study was to evaluate endothelium-dependent and –independent vasodilation in a group of normotensive people classified on the basis of salt sensitivity.

Design and method: Data from 22 living kidney donors that participated in the donor screening protocol with subsequent donation were included in the present analysis. Endothelial function was measured by analysis of digital volume pulse (DVP) waveform obtained by Pulse Trace system. Reflection index (RI) obtained from DVP reflects the small-size arteries vascular tone (endothelial function). To assess endothelium dependent arterial vasodilation, 400 ug of salbutamol (Salb) was given by inhalation. To assess endothelium independent arterial vasodilation, 300 ug of nitroglycerin (NTG) was administered sublingually. The arterial vasodilation, dependent on or independent of endothelial function, was defined as the maximum difference in Δ RI between baseline and the post-Salb or post-NTG period, respectively.

Results: We studied 14SR and 8SS, there were no significant differences in terms of age (46,6 ± 7 vs 40,4 ± 9 years old) and anthropometric measurements between groups SR and SS (weight 67,5 ± 8 vs 72,6 ± 15 kg, height 1,62±0,1 vs 1,62±0,1 mts, BMI 25±5 vs 27±4 and waist circumference 91±8 vs 93±10 cm). In basal conditions there were significant differences in blood pressure between SR and SS group (111±11/70±8 vs 121±16/79±8 mmHg p< 0,02 respectively) but we did not find statistical differences between them in RI (71±9 vs 69±9%). The RI after Salb was higher in SS than in SR group (RI= 68±9 vs 56±13 p<0,02) but there was no statistical difference after NTG (42±12 vs 40±13 % p=0,74). The arterial vasodilation, dependent on endothelial function, was significantly lower in SS than in SR group (Δ RI b/Salb 4±12 vs 22±16% p<0,02). We did not find significant differences between groups in the arterial vasodilation independent of endothelial function (34±15 vs 43±18% p=0,24).

Conclusions: Although the vascular tone of small-size arteries was similar between SS and SR in basal conditions, the endothelial function decreased significantly in SS healthy people.

PP.07.17 IS PULSE WAVE VELOCITY A VALUABLE TOOL IN THE DIAGNOSIS OF ENDOTHELIAL DYSFUNCTION IN PREHYPERTENSION?

H. Marcoyannopoulou Fojas [1], V.P. Podpalov [2], G.M. Fojas [1], O. Zhurova [2], N. Balashenko [2], O. Podpalova [2]. *[1] Philippine Department of Science and Technology, Taguig City, PHILIPPINES, [2] Vitebsk State Medical University, Internal Diseases Department, Vitebsk, BELARUS*

Objective: To show by Pulse Wave Velocity (PWV) determination and endothelium-dependent vasodilatation (EDVD) that prehypertension produces endothelial dysfunction and therefore should be managed.

Design and method: Pulse Wave Velocity was determined in normal, prehypertensive and established hypertensive clinically asymptomatic Belarussian subjects, by a non invasive method giving reproducible results (BPULS device) using the left external carotid and left dorsalis pedis arteries as central and peripheral points respectively, The arterial pulses were picked up by infrared sensors and recorded on a computer simultaneously with a single lead ECG. The time delay between the two pulses is determined. A shorter time delay or faster Pulse Wave Velocity indicates decreased arterial wall elasticity. Endothelium-dependent vasodilatation (EDVD) was assessed by measuring the responses of forearm blood flow to reactive hyperemia by venous occlusion plethysmography.
MATERIALS: A total of 155 clinically asymptomatic Belarussian subjects were examined. Age range - 30 to 65 years. Of this total, 21 had normal BP (120/80 or lower); 58 had prehypertension (Systolic - 121-140, Diastolic - 81-90); and, 76 were definitely established hypertensives (Systolic - >140 Diastolic - >90).

Results: Pulse Wave Velocity was increased in patients with prehypertension and established hypertension (10.9±0.4 m./sec., p <0.01; 11.3±0.3 m./sec., p <0.01, respectively) in contrast to normotensive individuals (9.3±0.4 m./sec). Endothelium-dependent vasodilatation was lower in patients with prehypertension and established hypertension (25.1±2.5%, p <0.05; 21.0±2.1%, p <0.05, respectively) in comparison with normotensive individuals (31.7±6.1%).
Endothelial dysfunction is associated with decreased arterial wall elasticity. Our study showed significantly decreased arterial elasticity even in prehypertensives compared to normotensives as shown by increased or faster PWV, This implies that arterial wall changes leading to arteriosclerosis already occur in prehypertension. Therefore these cases should be controlled by adapting healthy life style.

Conclusions: Pulse Wave Velocity determination shows arterial wall changes indicative of endothelial dysfunction in cases of prehypertension so they have to be controlled by adapting healthy life style. Pulse Wave Velocity, therefore, is a valuable tool in diagnosing endothelial dysfunction in prehypertension.

PP.07.18 EFFECTS OF BLACK RASPBERRY ON VASCULAR ENDOTHELIAL FUNCTION AND LIPID PROFILES IN PATIENTS WITH METABOLIC SYNDROME

S. Hong [1], T. Lee [2], J. Kwon [2], T. Jeong [2]. *[1] Korea University Anam Hospital, Seoul, SOUTH KOREA, [2] Gochang Black Raspberry Research Institute, Gochanggun, SOUTH KOREA*

Objective: Black raspberry (Rubus occidentalis) has been known for its anti-inflammatory and anti-oxidant effects. However, short-term effects of black raspberry on vascular endothelial function and lipid profiles have not been investigated in patients with metabolic syndrome.

Design and method: Patients with metabolic syndrome (n=77) were prospectively randomized into the black raspberry group (n=39, 750mg/day) and placebo group (n=38) during the 12-week follow-up. Lipid profiles, brachial artery flow-mediated dilatation (baFMD), circulating levels of endothelial progenitor cells such as CD34/KDR+, CD34/CD117+, CD34/CD133+ cells, and inflammatory cytokines such as IL-6, TNF-alpha, high sensitive C-reactive protein, adiponectin, ICAM-1, VCAM-1 were measured at baseline and at 12-week follow-up.

Results: Decreases from baseline in total cholesterol levels (-22.8±30.4mg/dL vs. -1.9±31.8mg/dL, p<0.05, respectively) and total cholesterol/HDL ratio (-0.31±0.64 vs. 0.07±0.58, p<0.05, respectively) were significantly greater in the black raspberry group when compared to the placebo group. Increases in baFMD at 12-week follow-up were significantly greater in the black raspberry group when compared to the placebo group (0.33±0.44mm vs. 0.10±0.35mm, p<0.05, respectively). Moreover, decreases from baseline in IL-6 (-0.4±1.5pg/mL vs. -0.1±1.0pg/mL, p<0.05, respectively) and TNF-alpha levels (-2.9±4.7pg/mL vs. 0.1±3.6pg/mL, p<0.05, respectively) were significantly greater in the black raspberry group. Increases in circulating levels of CD34/CD133+ cells were significantly greater in the black raspberry group when compared to the placebo group (19±109/uL vs. -28±57/uL, p<0.05, respectively) during the 12-week follow-up.

Conclusions: The use of black raspberry significantly decreased serum total cholesterol levels and inflammatory cytokines with increases in circulating levels of CD34/CD133+ cells, thereby improving vascular endothelial function in patients with metabolic syndrome during the 12-week follow-up.

PP.07.19 ANDROGENS MODULATE ENDOTHELIAL NITRIC OXIDE PRODUCTION IN HUMAN ENDOTHELIAL CELLS

D. Perez-Cremades [1], C. Alite [1], X. Vidal-Gomez [2], A. Mompeon [1], C. Bueno-Beti [2], S. Novella [1,2], C. Hermenegildo [1,2]. *[1] Dept. Physiology, Univ. Valencia, Valencia, SPAIN, [2] INCLIVA Biomedical Research Institute, Valencia, SPAIN*

Objective: Endothelial cells express androgen receptors and, therefore, are target of sex steroids. Endothelial cells release vasoactive compounds such as nitric oxide (NO). NO is the main regulator of vascular homeostasis and adequate levels are critical in the maintenance of a correct vascular physiology. NO bioavailability is key on sex vascular differences. Thus, the aim of this study is to investigate the effects of androgens on endothelial cells NO production to evaluate the different contribution of sex steroids in vascular biology.

Design and method: Primary human umbilical vein endothelial cells (HUVEC) were grown in EBM-2 medium (Lonza) and were exposed to physiological (1-100 nM) concentrations of testosterone and dihydrotestosterone (DHT) for 24 hours. Bicalutamide (1μM), an androgen receptor antagonist, was used to confirm androgen receptor contribution. NO production was measured with DAF-FM in an inverted fluorescence microscope (Nikon). Protein cuantification was determined by immunoblotting using specific antibodies for eNOS and Akt (Cell Signaling). ANOVA test and then Bonferroni's test were performed. Data are expressed as a percentage of control values as mean ± SEM.

Results: Androgens increase endothelial NO production at low concentration. Testosterone 1nM increased NO production up to 153±17% ($p<0.05$ vs. control) after 24 hours of exposure. DHT exerted a similar effect on NO production by increasing it to 128±13% at 1 nM ($p<0.05$ vs. control). Protein expression of eNOS (136±3%) and Akt (123±5%) was increased in endothelial cells by testosterone exposition. DHT also increased eNOS (185±8%) in HUVEC. These effects were mediated through the androgen receptor since were abolished by bicalutamide.

Conclusions: Testosterone and DHT, through the androgen receptor, increase NO production in HUVEC through an up-regulation of Akt-eNOS pathway.

PP.07.20 THE INFLUENCE OF HIGH SALT INTAKE ON VASCULAR RESPONSES OF MIDDLE CEREBRAL ARTERIES TO FLOW-INDUCED DILATION OF SPRAGUE-DAWLEY RATS

I. Grizelj, A. Cavka, Z. Mihaljevic, I. Drenjancevic. *Faculty of Medicine, Department of Physiology and Immunology, University of J.J. Strossmayer, Osijek, CROATIA*

Objective: Sprague-Dawley (SD) rats on high salt diet (HSD) remain normotensive and exhibit impaired relaxation responses to acetylcholine and hypoxia, as well as normotensive women on HSD, while there are no data of HSD effect on the flow-induced dilation (FID). The aim of the present study was to determine the effect of high salt intake on microvascular responses to flow-induced dilation in SD rats.

Design and method: 19 male SD rats were divided in two groups: a) control group (N=10) and b) group of rats on HSD for 7 days (4% NaCl; N=9). Prior to decapitation, rats were anesthetized with 75 mg/kg ketamine+2.5 mg/kg midazolam. Middle cerebral arteries were isolated and cannulated (DMT pressure myograph) for vascular reactivity measurements in response to stepwise increase in pressure (Δ 10- Δ 100), in the absence/presence of the NOS inhibitor L-NAME, COX-1,2 inhibitor indomethacin (INDO), selective inhibitor of microsomal CYP450 epoxidase activity MS-PPOH, and superoxide dismutase mimetic TEMPOL. To test differences among groups Two-way ANOVA was used, $p<0.05$ considered significant.

Results: FID was reduced in HSD group at each pressure gradient, but significantly at Δ 40, Δ 60 ($P<0.001$) and Δ 100 ($P<0.05$). The presence of L-NAME, INDO and MS-PPOH (independantly) significantly reduced FID in the control group at each pressure gradient ($P<0.05$) except Δ 10. L-NAME and INDO reduced FID in HSD group, but L-NAME significantly reduces FID at Δ 20 and Δ 40 ($P<0.05$). The presence of TEMPOL restores FID in HSD group to control levels at pressure gradients Δ 20- Δ 100 ($P<0.05$), while in control group TEMPOL had no effect.

Conclusions: These results demonstrate that: 1) High salt intake impaires vascular responses to FID; 2) Reactive oxygen species - superoxide anion radical (O2-) may contribute to impaired FID in rats on high salt diet; 3) Mechanisms of FID are different in control and HSD groups – while NO mediates FID in both groups of rats, metabolites of COX-1,2, and EETs could also contribute to FID in control group of rats.

PP.07.21 EFFECTS OF 12WK FLAVANOL-RICH COCOA ADMINISTRATION ON VASCULAR FUNCTION, BLOOD PRESSURE AND RENIN-ANGIOTENSIN SYSTEM IN HEALTHY SUBJECTS

D. Grassi [1], G. Desideri [1], M. De Feo [1], E. Fellini [1], F. Mai [1], A. Dante [1], S. Di Agostino [1], P. Di Giosia [1], K. Konouklas [1], L. Allegaert [2], H. Bernaert [2], C. Ferri [1] *[1] University of L'Aquila, L'Aquila, ITALY, [2] Barry-Callebaut, Lebbeke-Wieze, BELGIUM*

Objective: Cocoa flavonoids exert beneficial vascular effects and reduce the risk of cardiovascular morbidity and mortality.
To give an insight into the potential benefits deriving from cocoa even in prolonged periods of intervention, we tested the long term effects of low dose flavanol-rich and flavanol-free cocoa on office blood pressure (BP) levels, endothelium-dependent vasorelaxation, arterial stiffness and renin-angiotensin system (RAS) activity in healthy subjects.

Design and method: 25 healthy subjects were randomly and double-blindly assigned to receive low dose (20 g - 200 mg flavonoids) flavanol-rich or flavanol-free cocoa for 12 wks. Then, they will be crossed over for the other treatment. Treatments were separated by a one-week washout. The daily intake of dark chocolate (flavanol-rich or flavanol-free cocoa) varied a double blind, randomized, balanced cross-over design. Measurements (FMD, office BP, and PWV) were evaluated on baseline starting study and every 4 weeks of dark chocolate ingestion.

Results: Compared with control, flavanol-rich cocoa significantly increased FMD (from baseline 5,5±1,7% to 7.2±2.3%, to 7.1±2.1 and to 7.0±2.2% after 1, 2 and 3 months, respectively, $p<0.05$). The active treatment reduced office systolic and diastolic BP (from 117±14.6/68.1±8.7 mmHg to 110.3±10.1/63.5±6.62 mmHg, to 110.2±9.5/67.4±7.7 mmHg, to 111.2±9.7/66.6±6.0 mmHg after 1, 2 and 3 months of treatment, respectively, $p<0.05$). PWV significantly decreased after 3 months of treatment with flavanol-rich cocoa (from 6.7±1.3 m/s to 5.99±1.0 m/s), while no significant changes were reported in the control phase. No significant changes were observed on RAS activity.

Conclusions: Our findings indicate low dose flavanol-rich cocoa exerts significant effects on FMD, BP, arterial stiffness and wave reflection. These effects were observed in a longer-term investigation, maintaining the improvement during the intake for 3 months. The robust nature of our randomized, controlled, double-blind, crossover study design indicates dark chocolate ingestion, without additional calorie intake, can be reasonably incorporated into a dietary approach representing a consistent tool in cardiovascular prevention.

PP.07.22 ENDOTHELIAL FUNCTION IS IMPAIRED IN CONDUIT ARTERIES OF PANNEXIN1 KNOCKOUT MICE

D. Gaynullina [1], O.O. Kiryukhina [1], O.S. Tarasova [1,2], V.I. Shestopalov [3,4], Y. Panchin [5,6]. *[1] Faculty of Biology, M.V. Lomonosov Moscow State University, Department of Human and Animal Physiology, Moscow, RUSSIA, [2] State Research Center of the Russian Federation, Institute for Biomedical Problems RAS, Moscow, RUSSIA, [3] Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami, Miller School of Medicine, Miami, FL, USA, [4] Vavilov Institute of General Genetics, Russian Academy of Sciences, Moscow, RUSSIA, [5] Institute for Information Transmission Problems, Russian Academy of Sciences, Moscow, RUSSIA, [6] Department of Mathematical Methods in Biology, Belozersky Institute, M.V. Lomonosov Moscow State University, Moscow, RUSSIA*

Objective: Vertebrate pannexins were discovered as homologs to invertebrate gap junction proteins (innexins). Pannexins were shown to participate in numerous physiological or pathological processes, but their role in vascular tone regulation is currently not completely understood. Pannexin1 is the main pannexins isoform expressed in murine arterial network, but the role this isoform plays in vascular tone regulation remains unclear.

Design and method: Quantitative PCR was performed to evaluate the levels of mRNA expression in endothelium-intact and endothelium–denuded murine saphenous arteries. We studied isometric contractions to alpha1-adrenoceptor agonists or high-K+ depolarization and acetylcholine-induced dilation of saphenous arteries of wild type and Pannexin1 knockout mice.

Results: Our data demonstrate that Pannexin1 is expressed predominantly in endothelium, but not smooth muscle of saphenous artery. Our functional measurements showed that genetic ablation of Pannexin1 significantly impaired the ability of endothelium-intact saphenous arteries for dilation to acetylcholine and increased contractile responses to a variety of stimuli such as alpha1-adrenoceptor agonists and high-K+ depolarization, the effect was not seen in endothelium-denuded arteries.

Conclusions: These findings suggest that Pannexin1 (i) serves as one of the important players in the regulation of endothelial influences on arterial tone and (ii) facilitates vessel dilation and attenuates constriction.

PP.07.23 MICROPARTICLES AND HYPERTENSIVE CARDIOVASCULAR DISEASE: EFFECTS OF ANTIHYPERTENSIVE AND LIPID-LOWERING THERAPY ON CIRCULATING MICROPARTICLES

C. França [1], N. Massunaga [2], J. Do Amaral [1], M. Izar [2], C. Ferreira [2], H. Bianco [2], J. Kato [2], F. Fonseca [2]. *[1] Federal University of São Paulo, Medicine Department, Cardiology Division and Santo Amaro University, São Paulo, BRAZIL, [2] Federal University of São Paulo, Medicine Department, Cardiology Division, São Paulo, BRAZIL*

Objective: To evaluate the effects of rosuvastatin with or without valsartan, in patients ramdomly assigned to antihypertensive therapy with amlodipine or hydrochlorothiazide, in the circulating levels of microparticles, now recognized as biomarkers of vascular disease. The study was aimed to verify the effects of antihypertensive therapy on these new biomarkers alone and combined with other recognized therapies related to vascular protection (renin-angiotensin system blocker and statin).

Design and method: This was an open label, randomized, parallel-designed study with blinded endpoints. The patients were consecutively treated for a 4-week therapies (T1-T4) with quantification of microparticles at the end of each therapy. Platelet microparticles (PMP), monocyte microparticles (MMP) and endothelial microparticles (EMP) were quantified by flow-cytometry. T1 - patients under amlodipine 5 mg or hydrochlorothiazide 25 mg daily, alone; T2 - same T1 therapies with valsartan 160 mg added in both arms; T3 – same T2 therapies with rosuvastatin 20 mg added in both arms; T4 – same T3 therapies without rosuvastatin.

Results: There were no differences in arterial blood pressure (systolic and diastolic) between treatments based in amlodipine or hydrochlorothiazied throughout the study. After comparisons between groups (Mann-Whitney test), there were higher levels of MMP (p= 0.01) in the amlodipine group after T1 and higher levels of PMP in the same group after T4 (p= 0.003).
Conclusions: Despite similar blood pressure levels achieved, the choice of antyhypertensive therapy affects the circulating levels of microparticles. The concomitant use of statins and blockers of the renin-angiotensin system can reverse these differences.

PP.07.24 EFFECT OF XIONGDAN ON BLOOD PRESSURE, MESENTIRIC VASCULAR STRUCTURE AND FUNCTION IN SPONTANEOUSLY HYPERTENSIVE RATS

Z. Fang [1], L. Xie [2]. *[1] Fujian Hypertension Research Institute, Fuzhou, CHINA, [2] First Affiliated Hospital of Fujian Medical University, Fuzhou, CHINA*

Objective: To study the effect of Xiongdan on blood pressure, mesenteric vascular structure and function in Spontaneously Hypertensive Rats (SHRs).

Design and method: 24 male SHRs of 12 wks old were randomly divided into 3 groups: Xiongdan (SHR-X, n=8, A Chinese traditional herbal compound,800mg•kg-¹•d-¹), Rosuvastatin treated(SHR-R, n=8, 10mg•kg-¹•d-¹) and untreated controls(SHR, n=8,). Age- and weight-matched WKY rats served as controls(WKY, n=8). Systolic blood pressure (SBP) were measured by tail-cuff method at 0,4 and 8 wks after treatment. Serum 25-Hydroxyvitamin D(25(OH) D) was determined by ELISA. Wall to lumen area ratios(W/L) and the thickness of the wall to the radios of the lumen (TW/R1) in mesenteric arterioles(3rd grade branch) were assessed by morphormetic assay. Endothelium-dependent relaxation (EDdR), endothelium-independent relaxation (EDiR) were measured by PowerLab biological signal analytical system.

Results: SBP in X treated rats was significantly lower than that in untreated rats.[baseline in mmHg: (187.00±1.92) VS (190.91±2.93), P>0.05; 4 wks: (176.80±6.77)VS (199.58±5.71), P<0.05;8 wks: (169.42±4.52) VS (189.87±3.55), P<0.01].
SBP was higher than that in WKY during whole treatment period.Compared with SHR, Serum 25(OH)D is higher after 8 wks of X and R treated.[(6.81±1.59)(4.86±0.75) VS (3.15±0.33) ng/ml, P<0.01, respectively], but didn't reach the level of that in WKY. W/L and TW/R1 of mesenteric arterioles (3rd grade branch) in X and R treated rats were markedly lower than those of untreated SHR (P<0.001), and almost to the level of WKY(P>0.05). EDdR and EDiR of mesenteric arterioles (3rd grade branch) were increased in X and R group (both P<0.01, VS SHR).

Conclusions: The long-term therapy of Xiongdan may result in lowered blood pressure in SHRs, increase the plasma level of 25(OH)D, ameliorate the vascular structure and function.

PP.07.25 RELATIONSHIP AMONG OXIDATIVE STRESS, VASCULAR REACTIVITY CHANGES AND BLOOD PRESSURE IN HYPERTENSIVE PATIENTS ON AT1R ANTAGONIST THERAPY

I. Drenjancevic [1], M. Mihalj [1], R. Tadzic [2], M. Zulj [1], A. Vcev [1,3]. *[1] Faculty of Medicine University Josip Juraj Strossmayer, Osijek, CROATIA, [2] Gesundheitszentrum Lange Reihe Dr. Tadzic und Kollegen, Hamburg, GERMANY, [3] Clinical Hospital Center Osijek, Osijek, CROATIA*

Objective: The aim of this study was to assess the effects of AT1-receptor antagonisms on the markers of oxidative stress and endothelial activation in relation to vascular function and arterial blood pressure (ABP) changes in hypertensive patients.

Design and method: 30 newly discovered hypertensive subjects of both sexes received AT1 antagonist (olmesartan, 10-20mg/day) during 8 weeks. At the beginning and 8 weeks after therapy flow-mediated dilation (FMD) of brachial artery (BA) was measured by ultrasound (Acuson Siemens X300; ultrasound probe VF10-5; 105 MHz). The BA diameter, relative change in the diameter (δr) and percentage of diameter change (FMD%) were calculated for pre-occlusion, and after occlusion duration for 1, 2 and 3min. Serum levels of 8-iso-prostaglendin F2-alpha (8iPGF2α), endoglin and sICAM-1, sVCAM-1 and E-selectin were assessed by commercial ELISA kits. Paired t-test, or t-test were used as appropriate with Pearson's correlation calculated; p<0.05 was significant (SigmaPlotv.11).

Results: Eight weeks after therapy, ABP was significantly reduced (<=139/89mmHg; p<0.001). sICAM-1 and sVCAM-1 levels were significantly increased and positively correlated to BP whereas sE-selectin was decreased and negatively correlated to BP. Although 8iPGF2α and endoglin levels did not significantly change, there was significant positive correlation between 8iPGF2α and diastolic BP (p=0.0383), as well as between endoglin and 8iPGF2α (p=0.0477). The BA diameter was significantly bigger at all measured points compared to pre-therapy values; δr was significantly reduced after 3min, and FMD% after 2 and 3min of occlusion. δr positively correlated to systolic (SBP) and diastolic (DBP) after 2 and 3 min. FMD% positively correlated to SBP after 3min, and to DBP after 2min of occlusion. 8iPGF2α positively correlated to FMD% after 1 and 2 min occlusion duration; and to delta r after 1min of occlusion.

Conclusions: Blood vessels were relaxed after therapy due to decreased BP leading to less vigorous FMD response. Level of oxidative stress affected FMD. Endoglin might be a new marker of endothelial dysfunction in systemic hypertension, related to the level of oxidative stress and AT1 receptors' function. Results suggest permissive role of AT1 receptors in maintaining normal vascular function despite BP normalization.

PP.07.26 SYMPATHETIC PREDOMINANCE IS ASSOCIATED WITH IMPAIRED ENDOTHELIAL PROGENITOR CELLS AND TUNNELING NANOTUBES IN CONTROLLED-HYPERTENSIVE PATIENTS

E.M. Cavanagh [1,2], S.A. Gonzalez [1,2], F. Inserra [1], P. Forcada [1,2], C. Castellaro [1,2], J. Chiabaut-Svane [1,2], S. Obregón [1,2], M.J. Casarini 1, P. Kempny [1], C. Kotliar [1,2]. *[1] School of Biomedical Sciences, Austral University, Derqui, ARGENTINA, [2] Arterial Hypertension Center, Cardiology Department, Austral University Hospital, Derqui, ARGENTINA*

Objective: Bone marrow-derived endothelial progenitor cells (EPCs) contribute to the repair and regeneration of the injured endothelium. Two distinct types of EPC have been identified by in vitro cell culture of the blood mononuclear cell fraction: early-EPC, that promote vascular repair by releasing key cytokines, and late-EPC by differentiating into endothelial cells and incorporating into blood vessels. Also, early- and late-EPC can rescue damaged endothelial cells by transferring organelles through tunneling-nanotubes (TNT). In rodents, EPC-mobilization from the bone marrow depends on sympathetic nervous system activity. Indirect evidence suggests a relation between autonomic derangements and human EPC-mobilization. In this context, we aimed at testing whether hypertension-related autonomic imbalances are associated with EPC impairment.

Design and method: Thirty controlled-essential hypertensive patients [SBP/DBP=130(120-137)/85(61-88) mmHg; 81.8% male], and twenty-healthy normotensives [(114(107-119)/75(64-79) mmHg; 80% male] were studied. Mononuclear cells were cultured on fibronectin- and collagen-coated dishes for early-EPC and late-EPC, respectively. Low-(LF) and high-frequency (HF) components of short-term heart rate variability were analyzed during a 5-min rest, an expiration/inspiration maneuver, and a Stroop color-word-test. Modulations of cardiac sympathetic and parasympathetic activities were evaluated by LF/HF (%) and HF-power (ms2), respectively.

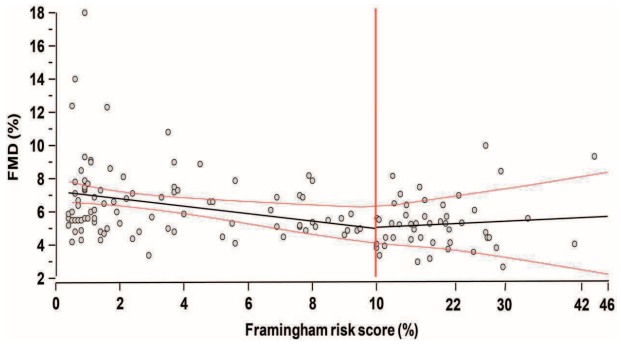
Results: In controlled-hypertensive patients, the numbers of early-EPC, early-EPC that emitted TNT, late-EPC and late-EPC that emitted TNT were 41%, 77%, 50% and 88% lower than in normotensives ($p<0.008$). In controlled-hypertensive patients, late-EPC number was positively associated with cardiac parasympathetic reserve during the expiration/inspiration maneuver (Rho=0.45, p=0.031) and early-EPC with brachial flow-mediated dilation (Rho=0.655; p=0.049); also, late-TNT number was inversely related to cardiac sympathetic response during the stress-test (Rho=-0.426, p=0.045). EPC exposure to epinephrine or norepinephrine showed negative dose-response relationships on cell adhesion to fibronectin and collagen; both catecholamines stimulated early-EPC growth, but epinephrine inhibited late-EPC growth.

Conclusions: In controlled-hypertensive patients, sympathetic overactivity/parasympathetic underactivity were negatively associated with EPC, suggesting that reducing sympathetic/increasing parasympathetic activation might favor endothelial repair.

PP.07.27 ASSOCIATION BETWEEN ENDOTHELIAL FUNCTION AND CARDIOVASCULAR RISK

A. Cardona, F. Angeli, A. Mengoni, A. D'Antonio, M. D'Ammando, G. Nucci, E. Sorbo, M. Bentivoglio, G. Ambrosio. *Division of Cardiology and Cardiovascular Pathophysiology, Teaching Hospital S.M. della Misericordia, Perugia, ITALY*

Objective: Endothelial dysfunction has been recognized as a surrogate marker of atherosclerosis. Flow-mediated-dilatation (FMD) is the most widely used non-invasive ultrasound method to asses endothelial function. However, the association between FMD and different levels of cardiovascular risk profile, as estimated by well-established risk scores in clinical practice, is still controversial.



Design and method: We included in our analysis 149 patients without previous cardiovascular events (mean age 45 ± 15; male subjects: 55%) referred to our laboratory for cardiovascular risk stratification. Using current guidelines, FMD was determined as percentage change of diameter in the brachial artery before and after cuff occlusion. The 10-year risk of cardiovascular events was estimated based on the Framingham risk score (FRS). Association between FMD and FRS was computed according to change point regression models.

Results: Overall, FMD was significantly associated with FRS ($r=0.33$, $p<0.001$). Nevertheless, using change point regression models (Figure), the significant association between FMD and FRS observed in patients with low-intermediate cardiovascular risk (FRS < 10%; p=0.010) was lost in patients with FRS >= 10% (p=0.435; Davies' test for change in the slope: $p<0.0001$).

Conclusions: Only in subjects at low-intermediate risk (FRS<10%), endothelial function estimated by FMD is related to 10-year cardiovascular risk. Our results suggest that the accuracy of ultrasonographic assessment of FMD as a measure of endothelial function is hampered in subjects with increased risk.
Conclusions: The combination of original perindopril/indapamide and simvastatin has advantages according to elimination of endothelial dysfunction and MAU and dominates from pharmacoeconomic point of view.

PP.07.28 CHOLECALCIFEROL SUPPLEMENTATION RESTORES ENDOTHELIAL FUNCTION IN ESSENTIAL HYPERTENSIVE PATIENTS WITH HYPOVITAMINOSIS D

L. Ghiadoni [1], D. Carrara [1], R.M. Bruno [2], M. Barzacchi [1], K. Raimo [1], F. Gervasi [1], A. Bacca [1], E. Duranti [1], S. Taddei [1], G. Bernini [1]. *[1] Departmentof Clinical and Experimental Medicine, University of Pisa, Pisa, ITALY, [2] Institute of Clinical Physiology, CNR, Pisa, ITALY*

Objective: Hypovitaminosis D has been associatd with increased cardiovascular risk, but whether the effects of its supplementation on cardiovascular endpoints are still poorly studied. Aim of this study was to investigate the effect of cholecalciferol supplementation on vascular function and structure in essential hypertensive patients with hypovitaminosis D.

Design and method: 27 consecutive patients (11 men, mean age 49±15yr, age range 22-73yr, BMI 27±4 Kg/m2) with essential hypertension and hypovitaminosis D (defined as plasma 25(OH)D values<30ng/ml) underwent oral supplementation with cholecalciferol 50000 I.U./week for two months. At baseline and at the end of the study, endothelium-dependent (flow-mediated dilation, FMD) and –independent (glyceril trinitrate 25 mcg s.l.) vasodilation were obtained. Central BP, wave reflection (Augmentation index, AIx) and carotid femoral pulse wave velocity (PWV) were assessed by applanation tonometry. Plasma vitamin D levels (25(OH) D) were also evaluated.

Results: After 2-month cholecalciferol administration, all patients normalized plasma 25(OH)D values (from 19±9 to 33±14 ng/ml, $p<0.001$). No changes in brachial BP (from 138±12/81±7 to 136±11/83±11 mmHg, p=ns) and central BP (from 127±14/82±7 to 126±13/84±12, p=ns) were observed. FMD was significantly increased after cholecalciferol supplementation (from 3.3±2.1 to 4.4±2.6%, $p<0.05$), in the presence of a similar brachial artery diameter (from 3.9±1.2 to 4.0±1.1mm, p=ns) and endothelium-independent vasodilation (from 8.3±4.4 to 8.4±4.2%). PWV and AIx were not significantly modified (from 7.8±1.6 to 7.5±1.5m/s and 22±14 to 23±13% respectively, p=ns).

Conclusions: Cholecalciferol supplementation in essential hypertensive patients with hypovitaminosis D is able to improve conduit-artery endothelial function.

PP.07.29 THE IMPROVEMENT OF ENDOTHELIAL FUNCTION UNDER THE INFLUENCE OF COMBINED ANTIHYPERTENSIVE AND HYPOLIPIDEMIC THERAPY

Y. Balandina, Y. Tarlovskaya, N. Maksimchuk-Kolobova. *Kirov State Medical Academy- Department of hospital Therapy, Kirov, RUSSIA*

Objective: To compare efficacy of combinations of antihypertensive and hypolipidemic medications in order to improve Endothelium-Dependent Vasodilation (EDVD), to eliminate Microalbuminuria (MAU) and also to calculate Cost-Effectiveness Ratio (CER).

Design and method: 78 patients with moderate arterial hypertension accompanied by type 2 diabetes with dyslipidemia were studied. The patients were randomized in groups A, B or C. Patients of group A (25 individuals) received original perindopril/indapamide and original simvastatin, patients of group B (30 individuals) - generic enalapril/indapamide and generic simvastatin, patients of group C (23 individuals) - original enalapril/hydrochlorothiazide and original simvastatin. The groups were comparable according to initial data ($p>0.05$). The target level of BP was considered to be <130/80 mm per Hg. The target level of LDL was considered to be <2 mmol/L. Office BP and LDL were examined every four weeks with a possible correcting of the therapy. Initially and within the 12 weeks EDVD (Method of Celermajer) and MAU (the semiquantitative method with test strips) were evaluated. CER was calculated as a ratio of cost (included only drug costs) to efficiency.

Results: By the 12th week of treatment all of the studied combinations have reduced both systolic and diastolic BP and also LDL ($p<0.05$). In group A 18 of 25 patients improved EDVD by>4.5%, in group B - 6 of 30 patients, in group C - 4 of 23 patients. The cost of improvement of EDVD by>4.5% was 6180.16 rubles/case in group A, 10794.1 rubles/case in group B and 18189.52 rubles/case in group C. By the 12th week of treatment MAU remained in 2 of 12 patients with initial nephropathy of group A, in 7 of 12 patients of group B and in 5 of 9 patients of group C. The cost of elimination of MAU was 5080.92 rubles/case in group A, 5384.52 rubles/case in group B and 6817.72 rubles/case in group C. CER A < CER B < CER C.

Conclusions: The combination of original perindopril/indapamide and simvastatin has advantages according to elemination of endothelial dysfunction and MAV and dominates from pharmacoeconomic point of view.

POSTERS' SESSION

POSTERS' SESSION PS08
LARGE ARTERIES

PP.08.01 MECHANISMS OF IMPROVED AORTIC STIFFNESS BY AROTINOLOL IN SPONTANEOUSLY HYPERTENSIVE RATS

W. Zhou, M. Hong, K. Zhang, D. Chen, W. Han, W. Shen, D. Zhu, P. Gao.
Shanghai Institute of Hypertension, Shanghai, CHINA

Objective: This study investigates the effects on aortic stiffness and vasodilation by arotinolol and the underlying mechanisms in spontaneously hypertensive rats (SHR).

Design and method: The vasodilations of rat aortas, renal and mesenteric arteries were evaluated by isometric force recording. Nitric oxide (NO) was measured in human aortic endothelial cells (HAECs) by fluorescent probes. Sixteen-week old SHRs were treated with metoprolol (200 mg•kg-1•d-1), arotinolol (30 mg•kg-1•d-1) for 8 weeks. Central arterial pressure (CAP) and pulse wave velocity (PWV) were evaluated via catheter pressure transducers. Collagen was assessed by immunohistochemistry and biochemistry assay, while endothelial nitric oxide synthase (eNOS) and eNOS phosphorylation (p-eNOS) of HAECs or aortas were analyzed by western blotting.

Results: Arotinolol relaxed vascular rings and the relaxations were attenuated by Nω-nitro-L-arginine methyl ester (L-NAME, NO synthase inhibitor) and the absence of endothelium. Furthermore, arotinolol-induced relaxations were attenuated by 4-aminopyridine (4-AP, Kv channels blocker). Arotinolol produced more nitric oxide compared to metoprolol and increased the expression of p-eNOS in HAECs. These results indicated that arotinolol-induced vasodilation involves endothelium-derived NO and Kv channels. The treatement with arotinolol in 8 weeks, but not metoprolol, markedly decreased CAP and PWV. Biochemistry assay and immunohistochemistry showed that aortic collagen depositions in the arotinolol groups were reduced compared with SHRs with metoprolol. Moreover, eNOS phosphorylation was significantly increased in aortinolol-treated SHR compared with SHRs with metoprolol.

Conclusions: Arotinolol improves arterial stiffness in SHR, which involved in increasing NO and decreasing collagen contents in large arteries.

PP.08.02 CORRELATION OF INTIMA-MEDIA THICKNESS TO COGNITIVE IMPAIRMENT IN HYPERTENSIVE PATIENTS

T. Yaneva-Sirakova [1], R. Tarnovska-Kadreva [1], L. Traykov [2], J. Petrova [2], M. Gospodinova [1]. *[1] Medical University Sofia, Department of Internal Medicine, Cardiology Clinic, Sofia, BULGARIA, [2] Medical University Sofia, Department of Neurology, Sofia, BULGARIA*

Objective: Elevated intima-media thickness (IMT) is a sign of atherosclerosis and is associated with hypertensive target organ damage. We tested the hypothesis weather there is a correlation between IMT as a marker of large arteries damage and mild cognitive impairment (MCI) – a clinical manifestation of brain target organ damage in hypertensive patients.

Design and method: 81 hypertensive patients on combined medical treatment were included in the study: 14(17.28%) males and 67(82.72%) females. The mean age was 68.54±8.77 years and the mean hypertension history - 11.44±8.74 years. Minimal follow-up period was 6 months. All the patients underwent complete anamnesis and physical examination, basic laboratory screening, echocardiography, carotid ultrasound, office- and home measurement of blood pressure, ambulatory blood pressure monitoring. The neuropsychological tests, which were used to assess the patients initially and during the follow-up visit were: Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). SPSS 19 was used for the descriptive statistics, t-test and the correlation analysis.

Results: The mean results for IMT were: left 0.83±0.11 cm and right 0.84±0.12 cm. The group of patients with MCI assessed with both MMSE and MoCA had significantly ($p=0.002$ for the left and $p=0.04$ for the right) higher IMT values than the group of patients without MCI. If only MoCA was considered as a screening tool for MCI for its higher sensitivity, the result was corresponding. The patients with MCI had significantly ($p=0.006$ for the left and $p=0.002$ for the right) higher IMT values than those without MCI. When correlation analysis was used to assess the strength and the direction of the correlation IMT – neuropsychological tests' results, a significant ($p<0.05$) negative correlation was found. The higher the IMT for both sides, the lower the MMSE and MoCA results both during the inclusion and the follow-up evaluation.

Conclusions: IMT and MCI are correlated - the higher the IMT, the more exacerbated MCI. IMT could be a valuable tool to rise the suspicion of the clinician for detection of target organ damage (MCI), as well as its persistence during follow-up.

PP.08.03 DECREASES IN AMBULATORY DAY IMPUTED AORTIC-TO-BRACHIAL BLOOD PRESSURE AMPLIFICATION ARE ASSOCIATED WITH LEFT VENTRICULAR MASS REGRESSION INDEPENDENT OF AMBULATORY BRACHIAL PRESSURE

G. Norton, E. Libhaber, H. Booysen, M. Sibiya, P. Sareli, A. Woodiwiss. *University of the Witwatersrand, Schools of Physiology and Medicine, Johannesburg, SOUTH AFRICA*

Objective: The relative role of aortic versus brachial blood pressure (BP) in cardiovascular disease is uncertain. Previous studies may be confounded by office BP measurements. The impact of in-treatment decreases in ambulatory aortic BP on end-organ changes has not been determined.

Design and method: We applied an imputation equation for central aortic pulse pressure to ambulatory day BP values and assessed the relationship between in-treatment increases in the day aortic-to-brachial amplification ratio (PPamp) and decreases in echocardiographic left ventricular mass index (LVMI) independent of changes in day brachial BP in 173 mild-to-moderate hypertensives treated for 4 months.

Results: Ambulatory day brachial systolic/diastolic BP (mm Hg) (154±15/101±8 to 132±15/88±10, $p<0.0001$), ambulatory day brachial PP (mm Hg) (53±11 to 45±9, $p<0.0001$), ambulatory day aortic PP (mm Hg) (43±10 to 35±8, $p<0.0001$) and LVMI (g/m2.7)(60.3±18.4 to 51.5±13.6, $p<0.0001$) decreased and ambulatory day PPamp increased (1.28±0.24 to 1.37±0.63, $p<0.0001$) over the 4 month treatment period. With adjustments for baseline LVMI, baseline PPamp and either decreases in day brachial PP (partial r=-0.17, 95% CI=-0.32 to -0.01, $p<0.05$) or decreases in day systolic BP (partial r=-0.18, 95% CI=-0.33 to -0.01, $p<0.05$), in-treatment increases in day PPamp were independently associated with decreases in LVMI. The brachial BP-independent relationships between changes in PPamp and LVMI were as strong as the relations between treatment-induced decreases in 24-hour brachial PP and decreases in LVMI (partial r=0.15, $p<0.05$). No relations between treatment-induced decreases in day PP or 24-hour or day systolic BP and decreases in LVMI were noted.

Conclusions: Independent of changes in brachial BP, in-treatment increases in day PPamp are associated with decreases in LVMI in mild-to-moderate hypertension. These data provide support for a key role of aortic BP in mediating increases in LVMI.

PP.08.04 AMBULATORY DAY IMPUTED AORTIC-TO-BRACHIAL BLOOD PRESSURE AMPLIFICATION IS ASSOCIATED WITH LEFT VENTRICULAR MASS INDEPENDENT OF AMBULATORY BRACHIAL PRESSURE

A. Woodiwiss, H. Booysen, M. Sibiya, E. Libhaber, P. Sareli, G. Norton
University of the Witwatersrand, Schools of Physiology and Medicine, Johannesburg, SOUTH AFRICA

Objective: Aortic blood pressure (BP) may be considerably lower than brachial BP. Conflicting results characterize studies reporting on the relative role of aortic versus brachial BP in cardiovascular disease. These studies may be confounded by office measurements. The impact of ambulatory aortic BP has not been determined.

Design and method: We applied an imputation equation for central aortic pulse pressure (PPc) to ambulatory day BP values and assessed the relationship between day PPc or the day aortic-to-brachial amplification ratio (PPamp) and echocardiographic left ventricular mass index (LVMI) independent of day brachial BP in a community-based sample of African ancestry.

Results: The imputation equation (derived in 1179 randomly recruited participants from a community-based sample), produced PPc values which closely approximated PPc determined from radial tonometry and SphygmoCor software (r2=0.96, mean difference [±2xSD] =-1.4±6.2 mmHg). In 485 participants from the community sample, where day PPamp was noted to be 1.40±0.18, ambulatory day PPc (partial r=0.13, p<0.01) and PPamp (partial r=-0.09 to -0.10, p<0.05) were associated with LVMI independent of ambulatory day brachial PP or systolic BP and additional confounders. Ambulatory day brachial BP-independent relationships between day PPc or day PPamp and LVMI were similar in strength to independent relationships noted between ambulatory day brachial systolic BP (partial r=0.11, p<0.05) or PP (partial r=0.15, p<0.005) and LVMI (p>0.05 for comparison of relations).

Conclusions: Ambulatory day aortic PP and day aortic-to-brachial BP amplification are associated with LVMI independent of ambulatory day brachial BP. These data provide support for a key role of aortic BP in mediating increases in LVMI.

PP.08.05 WAVE REFLECTION DOES NOT DIFFER BETWEEN PATIENTS WITH NORMAL AND WITH SEVERELY IMPAIRED SYSTOLIC FUNCTION

T. Weber [1], S. Parragh [2], B. Hametner [2], M. Bachler [2], B. Eber [1], S. Wassertheurer [2]. *[1] Cardiology Department Klinikum Wels-Grieskirchen, Wels, AUSTRIA, [2] Austrian Institute of Technology, Vienna, AUSTRIA*

Objective: Non-invasive estimates of wave reflection are independent prognostic markers in patients with normal systolic function, showing a direct relationship between the extent of wave reflection and cardiovascular risk. In systolic heart failure, wave reflection indices, based on pulse wave analysis (PWA), are reduced, whereas prognosis is impaired as well, as compared to normal systolic function. We aimed to investigate the amount of wave reflection by means of PWA and wave separation analysis (WSA) in patients with severely impaired systolic function.

Design and method: Wave reflection parameters were derived from PWA and WSA, with non-invasively generated aortic pressure waveforms and Doppler flow measurements in 61 patients with reduced (rEF; mean EF was 28%) and 122 patients with normal ejection fraction (nEF; mean EF was 69%). Both groups were matched for age, gender, and brachial blood pressures. Additionally we compared these measures with WSA-estimates from 3 different flow models (triangular, averaged, Windkessel).

Results: Central systolic blood pressure and central pulse pressure tended to be lower, heart rate was significantly higher (by 9 beats/minute), and ejection duration was significantly shorter in rEF. Augmentation Index as well as Pressure Augmentation were significantly lower in patients with rEF.
After adjustments for heart rate and ejection duration, all parameters of wave reflection were comparable for patients with rEF and nEF (Table). WSA parameters assessed with the Windkessel based model were similar to those derived from Doppler flow. Triangular approximation showed comparable results to Doppler flow only for rEF in opposite to the averaged waveform.

		bSBP	bDBP	pPP	cPP	AP	P1	|Pf|	|Pb|	PP amp	AIx	RM
	rEF	124.8±20.3	78.6±13.4	46.2±1.9	33.1±1.6	6.9±0.9	26.8±1.4	24.6±1.0	13.9±0.7	144±2.1	18.1±1.3	56.3±1.5
	nEF	126.6±13.7	79.1±9.4	47.5±1.0	36.4±0.9	9.4±0.4	27.0±0.8	24.7±0.6	15.2±0.4	132±1.3	24.8±0.9	62.1±0.9
	p	0.35	0.78	0.30	0.02 *	0.0001 *	0.95	0.68	0.02 *	<0.0001 *	<0.0001 *	0.0005 *
HR, ED	rEF			48.5±1.8	36.7±1.5	9.2±0.7	27.3±1.4	26.3±1.0	15.6±0.6	136.7±1.9	21.9±1.4	58.6±1.4
HR, ED	nEF			46.4±1.2	34.6±1.0	8.3±0.5	26.8±0.9	23.8±0.7	14.4±0.4	135.7±1.2	23.0±0.9	61.0±1.0
HR, ED	p			0.38	0.30	0.34	0.77	0.06	0.14	0.68	0.56	0.20

bSBP, bDBP... brachial systolic and diastolic blood pressure; cPP...central pulse pressure; AP ... Pressure Augmentation; P1 ... incident pressure wave height; Pf, Pb ... amplitudes forward and backward wave; PP amp... PP amplification; AIx...Augmentation Index; RM...Reflection Magnitude; HR...heart rate; ED...ejection duration.

Conclusions: The amount of wave reflection in the arterial system does not differ between patients with normal and patients with severely impaired systolic function.

PP.08.06 THE INCREMENTAL EFFECT OF ALCOHOL CONSUMPTION ON REDUCED ARTERIAL ELASTICITY IN EASTERN EUROPEAN IMMIGRANTS

V. Katsi [1], G. Vamvakou [2], I. Felekos [1], N. Alexopoulos [3], C. Varounis [2], M. Daskalaki [4], C. Stefanadis [3], T. Makris [4], I. Kallikazaros [1].
[1] Hippokration General Hospital, Cardiology Clinic, Athens, GREECE, [2] Attikon General Hospital, Cardiology Clinic, University Medical School, Athens, GREECE, [3] Hippokration General Hospital, Cardiology Clinic, University Medical School, Athens, GREECE, [4] General Maternity District Hospital Elena Venizelou, Department of Cardiology, Athens, GREECE

Objective: The association between excessive alcohol consumption and cardiovascular (CV) risk is robust. Arterial stiffness is an established down-stream marker of CV risk.We assessed the hypothesis that possible different alcohol consumption patterns between first generation Eastern European immigrants and native Greeks reflect different vascular age in the above mentioned populations.

Design and method: We studied 67 immigrants with newly diagnosed untreated stage I-II essential hypertension (EH), (aged=51.5±15 years, 35 male, office blood pressure (BP)=158/92 mm Hg) coming from Eastern Europe to Greece within the previous two years and 61 EH natives matched for age, gender and office BP. Arterial stiffness was evaluated on the basis of carotid-femoral pulse wave velocity (c-f PWV). Current alcohol intake was assessed by responding to a question on how many alcohol units they consumed during the day (0, < 1, 1-2, 3-5 and >5 units/day).

Results: Hypertensive immigrants compared to natives exhibited significantly higher values of c-f PWV (8.4±0.3 vs 7.1±0.5 m/sec, p=0.003). A significant greater proportion of immigrants reported excessive alcohol intake compared to natives (18% vs 5%, p= 0.02 - Image). In the immigrants group, c-f PWV was positively associated with alcohol intake (r= 0.28, p=0.004).

Conclusions: Hypertensive immigrants in the setting of similar hemodynamic load are characterized by higher alcohol consumption and stiffer aorta compared to natives. This unfavourable BP profile may contribute to the disproportionate CV risk of this frail population.

PP.08.07 GLYCEMIC CONTROL IS ASSOCIATED WITH ARTERIAL STIFFNESS AND LEFT VENTRICULAR HYPERTROPHY IN HYPERTENSIVES

D. Terentes-Printzios, C. Vlachopoulos, G. Vyssoulis, P. Pietri, N. Ioakeimidis, M. Abdelrasoul, A. Aggelis, A. Aggelakas, K. Aznaouridis, C. Stefanadis
Peripheral Vessels Unit, 1st Cardiology Department, Hipokkration Hospital, Athens Medical School, Athens, GREECE

Objective: Hypertension is associated with left ventricular hypertrophy (LVH) and increased arterial stiffness, which are predictors of cardiovascular risk. Glycemic control, as assessed by hemoglobin A1c (HbA1c) levels, is an independent predictor of cardiovascular morbidity and mortality in hypertensives. We assessed the hypothesis that LVH and arterial stiffness are associated with glycemic control in never treated hypertensives.

Design and method: We enrolled 1225 consecutive essential hypertensives (mean age 52.9±11.7 years, 728 males, 86 diabetics). HbA1c was measured in venous blood samples. Left ventricular mass index (LVMI) was assessed by echocardiography. M-mode imaging was used for wall-thickness measurements. LVMI was calculated using the Devereux formula. LVH was defined as a LVMI>=125 g/m2 in men and >=110 g/m2 in women. Glomerular filtration rate (GFR) was estimated by the Cockcroft-Gault formula. Arterial stiffness was evaluated with carotid-femoral pulse wave velocity (cfPWV).

Results: In multivariable regression analysis, HbA1c exhibited significant positive association with LVMI and cfPWV, which was independent of age, gender, mean blood pressure, smoking habits, body-mass index, blood glucose, low-density lipoprotein, GFR and C-reactive protein (p=0.007, adjusted R2 of model=0.301 and p<0.001, adjusted R2 of model=0.418). HbA1c levels were significantly higher in patients with LVH compared with patients with normal ventricular mass (5.8 vs. 5.4%, respectively, P<0.001). In multivariable logistic regression models adjusting for the abovementioned confounders, HbA1c levels were significantly associated with LVH (OR=1.41, 95% CI:1.06-1.87, p=0.017) and cfPWV>=10m/s (OR=2.53, 95% CI:1.64-3.89, p<0.001).

Conclusions: Higher HbA1c is an independent predictor of increased LVM, arterial stiffness and LVH in essential hypertensives. These findings support the significance of adequate glycemic control in patients with hypertension regardless of the presence of diabetes.

PP.08.08 RELATION OF CARDIO-ANKLE VASCULAR INDEX, AN ARTERIAL STIFFNESS PARAMETER, TO CAROTID ATHEROSCLEROSIS IN HYPERTENSIVE PATIENTS

M. Takata, A. Shimakura. *Toyama Teishin Hospital, Toyama, JAPAN*

Objective: Cardio-ankle vascular index (CAVI), blood-pressure independent arterial stiffness parameter, has been accepted as a good surrogate marker of cardiovascular disease. However, the significance of blood pressure independency

among different arterial stiffness parameters is not fully understood. The aim of this study is to assess the relation of blood-pressure dependent and independent parameters of arterial stiffness to carotid atherosclerosis in hypertensive patients.

Design and method: Subjects were 725 outpatients with hypertension. CAVI, heart-ankle pulse wave velocity (haPWV) , brachial-ankle PWV (baPWV) and ankle-brachial pressure index (ABI) were measured by VaSera VS-1000 (Fukuda Denshi Co., Ltd.). HaPWV was measured by length and time difference between aortic valve and ankle using photocardiogram and pulse wave analysis. Accordingly, central aorta, abdominal, femoral and tibial arteries were involved in measured portion of haPWV. CAVI is pressure independent arterial stiffness parameter using stiffness parameter beta and Bramwell-Hill's equation. The intima-media thickness (IMT) of carotid arteries was measured by ultrasonography (Aloka Co., Ltd.). Both mean and maximum IMT were calculated as structural atherosclerosis parameters.

Results: Mean age of subjects was 68 y/o, and 345 patients were females. Mean CAVI, haPWV, baPWV and ABI were 8.81,8.25m/sec,14.61m/sec, and 1.11. Average of mean and max IMT were 0.754±0.150 mm and 1.735±0.826mm. Mean IMT was closely related to CAVI, haPWV and baPWV (0.338,0.326,0.280) , and max IMT was also related to CAVI, haPWV and baPWV (0.221,0.185,0.177). However, ABI was a weak parameter to assess carotid atherosclerosis (-0.125, -0.053 in mean and max IMT). There were also positively correlated among CAVI, haPWV and baPWV. Both systolic and diastolic blood pressures were closely related to PWVs, but not CAVI (0.162,0.568,0.485 and -0.018,0.404,0.304 in CAVI, haPWV and baPWV).

Conclusions: In hypertensive patients, CAVI was weakly affected by blood pressure and a strong parameter to assess structural changes of carotid arteries among measured arterial stiffness parameters. These results suggested that blood pressure correction is important to assess arterial stiffness in hypertensive patients.

PP.08.09 POSSIBILITIES OF HIGH-RESOLUTION VESSEL ULTRASOUND IN DIAGNOSIS OF INFLAMMATORY WALL CHANGES IN PATIENTS WITH TAKAYASU ARTERITIS AND ARTERIAL HYPERTENSION

M. Andreevskaya, O. Sivakova, N. Chikhladze, A. Rogoza, I. Chazova.
Russian Cardiology Research Complex, Moscow, RUSSIA

Objective: Investigation of aortic stiffness in patients with TA, and determination of its relation with disease activity.

Design and method: Twenty three female with TA at the age of 43±13 years were examined, the blood pressure (BP) level was 140±12/80±8 mm Hg. Disease activity was assessed by measurement of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Patients were treated with immunosuppressive therapy, with statins and with antihypertensive medications. The control group consisted of 34 normotensive volunteers (27 men and 7 women) at the age of 42±5 years, the BP level was 120±8/78±6 mm Hg. Aortic regional stiffness – pulse wave velocity (PWV) was evaluated by visualize ultrasonic methods (PHILIPS EnVisorHD). The results are presented as median and 25-75 percentile.

Results: Aortic PWV was significantly higher in TA patients 9,3 (7,6;11) m/s compared with control group 5,2(4,8;5,5) m/s (p<0,001). Aortic PWV in patients with active phase of the disease (n=8) was 11,2 (7,7;13,6)m/s compared with 8,6 (7; 10,6) m/s in patients with clinical remission (n= 15) (p= 0.19). PWV mildly correlate with CRP (r=0,42, p= 0.04) but not with ESR.

Conclusions: PWV mildly correlate with parameter of disease activity in patients with TA. Our data show the influence of inflammatory morphological processes on the aortic stiffness in patients with TA. But PWV could not be justified as a criterion of inflammatory process activity in the vessel wall.

PP.08.10 THE POSSIBILITIES OF DIFFERENT INSTRUMENTAL METHODS IN DIAGNOSIS OF EARLY INFLAMMATORY ARTERIAL CHANGES IN PATIENTS WITH TAKAYASU ARTERITIS

O. Sivakova, N. Chikhladze, S. Gaman, T. Balakhonova, M. Tripoten, E. Yarovaya, I. Chazova. *Russian Cardiology research complex, Moscow, RUSSIA*

Objective: Takayasu arteritis (TA) is a chronical inflammatory large-vessel vasculitis that occurs predominantly in young females. The diagnosis is not usually established before arterial stenoses or occlusions are present. The aim of our study to compare the posibilities of MSCT-angiography high-resolution vascular ultrasound in diagnosis of early inflammatory arterial changes in patients with Takayasu arteritis.

Design and method: 32 female with TA aged from 17 to 76 (42, 68±14,45) year were detected. The duration of TA amounted to 19.3±16.9 years. Ultrasound examinations of both common, internal, external carotid arteries, both subclavian arteries were performed to all patients (Acuson 128 XP 10 (Siemens, Germany), VIVID 7 (GE), iU-22 - Philips). MSCT-angiography (Aquilion 64, Toshiba, Japan) was made in 22 pts.

Results: Arterial hypertension (AH) was detected in 27 of 32 (84%) pts, blood pressure (163±11,6/92±12,3 mm Hg).The estimation the diagnostic significance of each method in the definition of the wall thikness of the common carotid arteries (CCA) was obtained by using statistical analysis. The hypothesis about absence of connection between the results obtained according to the MSCT angiography and ultrasound of high resolution was tested. Using Fisher's two-tailed test this hypothesis was rejected and the connection between the results obtained by ultrasound and MSCT angiography was statistically significant. Moreover, it was noted that the results of ultrasound and MSCT angiography on this criteria coincide 76.2% of cases and do not coincide in 23.8% of cases. As it turned out, in all the different cases ultrasound was a more precisely method than MSCT angiography (this hypothesis is tested by the criterion of McNemar x2, p=0,0003).

Conclusions: High-resolution vascular ultrasound is more accurate in the diagnosis of early changes in the CCA than MSCT in TA patients.

PP.08.11 PROGNOSTIC ROLE OF STRUCTURAL CHANGES OF LARGE ARTERIES AND PERIPHERAL BLOOD FLOW IN PATIENTS WITH CHRONIC HEART FAILURE

I. Shkurat. *NSC Institute of Cardiology, Kiev, UKRAINE*

Objective: To investigate the dependence of structure of a.femoralis (a.F) and peripheral blood flow (PBF) on severity and 12-months survival prognosis of chronic heart failure (CHF).

Design and method: Ultrasonography of a.F, a.dorsalis pedis (a.DP) were performed in 129 patients (age 56.6±1.2 years; 89 males) with stable CHF (NYHA II-III) and LVEF<40% and in 40 age-matched healthy subjects. Diameter (D), intima-media thickness (IMT) of a.F, velocities (Vps and Ved) in a.DP were measured; index of relative wall thickness (RWT) of a.F: RWT=IMT/D; index of peripheral resistance (RI): RI=(Vps-Ved)/Vps. Kaplan-Meier 12-months survival analysis was performed for RWT as well as for Vps, Ved, RI in a.DP based on «below median vs. above median» approach.

Results: In pts with CHF IMT and RWT were significantly higher (IMT: 0.99±0.16 vs. 0.59±0.09 mm, p<0.001; RWT: 0.16±0.03 vs. 0.10±0.01 unit, p<0.001). Vps and Ved in a.DP were significantly lower in pts with CHF (39.3±2.1 vs. 56.4±6.6 cm/s, p<0.01 and 5.2±0.8 vs. 12.9±1.7 cm/s, p<0.01, respectively), and RI in a.DP was significantly higher (0.83±0.04 vs. 0.77±0.02 unit, p<0.01). These changes become more pronounced in pts with NYHA class III-IV than in NYHA class II (Vps 32.3±1.9 vs. 35.7±2.1 cm/s, p=0.03, Ved 5.8±0.7 vs.6.9±1.3 cm/s, p=0.03 and RI 0.84±0.03 vs. 0.82±0.02 unit, p=0.04, respectively). Kaplan-Meier 12-months survival analysis was performed in relation to the RWT (p=0.038), Vps in a.DP (p=0.04), Ved in a.DP (p=0.037) and RI in a.DP (p=0.04). Significantly lower survival was apparent in pts with RWT>0.16, Vps<36 cm/s, Ved<6 cm/s, RI>0.84 unit.

Conclusions: The present study indicates that remodeling of peripheral blood vessels is accompanied by decrease peripheral arterial blood flow and by increase in resistance of resistive vessels in patients with CHF. RWT, Vps, Ved and RI in a. dorsalis pedis may be used for mortality risk stratification in patients with CHF.

PP.08.12 EFFECT OF IVABRADINE AND ATENOLOL ON CENTRAL HEMODYNAMICS IN HYPERTENSIVE PATIENTS AFTER MYOCARDIAL INFARCTION

A. Shavarov, G. Kiyakbaev, V. Moiseev, Z. Kobalava
Peoples Friendship University of Russia, Moscow, RUSSIA

Objective: We tried to compare effect of ivabradine in combination with atenolol (I+A) and atenolol (A) on central hemodynamics in hypertensive patients (pts) after myocardial infarction.

Design and method: The study included 40 hypertensive patients (88% male), mean age 63±8 years, with history of myocardial infarction and left ventricular systolic dysfunction. Two weeks before randomization all pts received atenolol 50 mg per day additionally to standard treatment. After that pts were randomly assigned to I (n=20) and A (n=20) dose up-titration for 2 weeks with achieving of target heart rate (HR) less 60 bpm at rest. Mean doses were 14,3 mg for I in I+A group pts and 135,8 mg in A group pts. Follow-up period was 12 weeks. Heart rate (HR), peripheral systolic blood pressure (SBP), central aortic systolic pressure

(CSP), carotid-femoral pulse wave velocity (PWV), AIx normalized for a heart rate of 75 bpm (AIx75), amplification of pulse pressure (APP) were estimated.

Results: HR decreased from 77 to 52 bpm with I+A and from 76 to 52 bpm with A (both p=0.001). SBP decreased by 4.0 mm Hg with I+A and by 10.0 mm Hg with A (p=0.03). CSP decreased by 7.0 mm Hg with I+A and 12.0 mm Hg with A (p=0.73). PWV decreased by 1.3 m/s after I+A and by 1.1 m/s after A (p=0.78). AIx75 decreased from 31 to 20% after I+A (p=0.001) and from 31 to 28% after A (p=0.06) 6 weeks after treatment and it then decreased to 16% in I+A group vs 23% in A group (p=0.001) when treatment ended. APP increased by 11% after I+A and it decreased by 11% after A (p=0.001).

Conclusions: Both I+A and A showed comparable reduction of HR, CSP and PWV. In contrast to atenolol combination of I+A was associated with more significant and faster decrease of AIx75 and increase of APP.

PP.08.13 ASSOCIATION OF LIPOPROTEIN APOA-I AND AORTIC STIFFNESS WITH PERIPHERAL ARTERIAL DISEASE: RESULTS OF A NINE-YEAR FOLLOW-UP

J. Seidlerová, J. Filipovský, O. Mayer Jr. *Dept. of Internal Medicine II, Faculty of Medicine, Charles University, Pilsen, CZECH REPUBLIC*

Objective: We investigate whether incidence of peripheral arterial disease (PAD) defined as ankle brachial index (ABI) <0.9 is independently associated with aortic stiffness and lipoprotein apoA-I (apoA-I) in elderly subjects free from PAD at baseline.

Design and method: The present study included 96 elderly lecture attendees ("Continuing Adult Education") who were examined at baseline and after a median follow-up of 9.5 years. We used multiple linear and logistic regression analyses to assess predictors of ABI decrease and PAD. As independent covariates we considered parameters with known effect on arterial stiffness or ABI and use of antihypertensive medication.

Results: At baseline, mean age was 67.2±4.9 years, 79.2% were women, 33.3% of subjects had arterial hypertension, and 5.2% diabetes mellitus. During follow-up, the ABI decreased (1.15±0.12 vs. 1.00±0.19; p<0.0001) and there were 27 (28.1%) incident cases of PAD defined as ABI<0.9. While accounting for covariates, decrease in ABI was associated with lipoprotein apoA-I (β = +0.045±0.018; p=0.017) and PWV (β=–0.038±0.017; p=0.025). Additional adjustment for antihypertensive treatment started during the follow-up weakened the association between PWV and ABI decrease (p=0.091). The incidence of PAD was associated only with apoA-I (OR 0.55, 95%CI 0.32 – 0.97; p=0.038). PWV was not significant predictor of incident PAD either in basically adjusted model or in model adjusted also for antihypertensive treatment (p>=0.082).

Conclusions: In elderly subjects without manifest PAD at baseline, the lipoprotein apoA-I and aortic stiffness are associated with the ABI decrease. However, antihypertensive treatment started during follow-up moderates effect of aortic PWV on ABI decrease.

PP.08.14 AORTIC DISTENSIBILITY IS AN INDEPENDENT DETERMINANT OF MYOCARDIAL DIASTOLIC FUNCTION

D. Rosenbaum [1], N. Kachenoura [2], A. Redheuil [2], A. Decesare [2], F. Villeneuve [1], X. Girerd [1], P. Cluzel [3]. *[1] Cardiovascular Prevention Unit, Pitié Salpêtrière Hospital, Paris, FRANCE, [2] Laboratoire d'Imagerie Fonctionnelle, UPMC INSERM U 678, Paris, FRANCE, [3] Département d'Imagerie Cardiovasculaire, Pitié Salpêtrière Hospital, Paris, FRANCE*

Objective: Hypertension causes increase in myocardial post load and in aortic stiffness. The aim of this study is to determine the relationship between aortic wall properties and left ventricle diastolic function.

Design and method: Cardiovascular magnetic resonance exam (1.5T Siemens) of the proximal aorta was performed. Ascending aortic diameters and strain were calculated using the ARTFUN software and an automated segmentation of SSFP cine acquisitions acquired in the axial view, during breath-holding, at the level of pulmonary bifurcation perpendicular to the aorta. Aortic strain was used to calculate aortic distensibility in each subject: distensibility (AD) =strain/cPP where cPP is the central pulse pressure obtained by tonometry (sphygmocor ®). The CARD-FLOW ® software allows a semi automated segmentation of transmitral and transaortic flows as well as myocardial septal wall velocities. Phase contrast ventricular sequences were analyzed to determine E, A, E'and A' waves velocities as well as Mitral Filling volume (Fv) Home Blood pressure (hBP) records were used to define BP levels. Carotido femoral pulse wave velocity (CfPWV) was assessed using just after MRI using Sphygmocor ®.

Results: Population included 55 treated hypertensives in primary prevention of mean age 53.4years and 16 normotensive controls matched for age/gender and body mass index. Male proportion was 55.5% and 50% of hypertensives had uncontrolled hBP (122/76 vs 150/94mmHg p<.01). AD differed between the 3 groups (p<.03): 33.2, 24.2 and 18.1 10-3kPa-1 in control subjects, controlled and uncontrolled hypertensives respectively. Cf-PWv differed between control subjects and uncontrolled hypertensives (10.4 vs. 11.8m/s p<.05).Diastolic parameters did not differ among groups. Univariate analysis showed strong association of AD and CfPWV with age (p<.001), central blood pressure and all diastolic parameters (E, E', E/A, E/E', A/Fv and E/Fv). Multivariate analysis showed after adjustment for age and central blood pressures that E' and A/Fv were independently linked to AD (p<.001) and that E' and E/E' were linked to CfPWV (p<.05).

Conclusions: In hypertension, Aortic stiffness indexes and especially AD are determinant of diastolic function independently of age and blood pressure levels.

PP.08.15 EXCESS PRESSURE IS INDEPENDENTLY RELATED TO MEASURES OF LV MASS AND CONCENTRIC GEOMETRY IN ESSENTIAL HYPERTENSION

G. Pucci [1], B. Hametner [2], F. Battista [1], F. Anastasio [1], S. Wassertheurer [2], G. Schillaci [1] *[1] Department of Medicine, University of Perugia, Internal Medicine, Santa Maria Hospital, Terni, ITALY, [2] AIT Austrian Institute of Technology, Health and Environment Department, Vienna, AUSTRIA*

Objective: According to the reservoir theory, arterial pressure can be decomposed as the sum of reservoir (Pres) and excess (Pexc) pressure. Pres is constant along the entire arterial tree and results in the minimum left ventricular (LV) hydraulic work, while excess pressure is linked to the excess work of the heart. However, data about the relationship of Pres and Pexc with cardiac structural features in hypertension are still lacking

Design and method: 446 never-treated hypertensive subjects (mean age 48±11 years, 62% men, BP 148/92±16/10 mmHg) were evaluated through M-mode and 2D-echocardiography. Aortic pressure waveform was derived from radial applanation tonometry (SphygmoCor). Amplitudes of Pres and Pexc were calculated using ARCSolver algorithms which are solely based on central pressure curves. LV mass was indexed to height^2.7, LV hypertrophy was defined as LV mass>51 g/m^2.7. Relative wall thickness (RWT) was expressed as: 2 x posterior wall thickness/LV internal diameter. Concentric geometry was considered if RWT>0.43. All subjects underwent 24-h automatic BP assessment (SpaceLabs 90207, 1 measure/15').

Results: Pexc and Pres were both positively correlated with LV mass (Pearson's r= 0.15 and 0.17, respectively, both p<0.01) and RWT (r=0.16, p<0.01; r=0.11, p=0.02). After adjustment for age, sex, body mass index and 24-h systolic BP, subjects with LV hypertrophy had significantly higher Pexc (18.4±10.3 vs 17.0±5.4 mmHg, p=0.02), but not Pres (39.8±12.6 vs 37.5±24.2 mmHg, p=0.09). In a multivariate model adjusting for multiple cardiovascular risk factors and other confounders, an increased Pexc independently predicted both LV mass (β=0.08, p=0.04, multiple R=0.58) and RWT (β=0.10, p=0.02, multiple R=0.40), while these relationship were not observed for Pres.
Conclusions: LV mass and RWT are linearly and independently associated to aortic excess pressure (Pexc), but not to reservoir pressure (Pres) in untreated hypertensive subjects, even after taking into account the effect of 24-hour systolic BP. Structural cardiac abnormalities may be related to an increase of excess pressure. These results confirm the close functional connections between properties of proximal large arteries and LV structural remodeling.

PP.08.16 ARTERIAL STIFFNESS AND CENTRAL AORTIC BLOOD PRESSURE IN SUBJECTS WITH SICKLE CELL DISEASE

M. Pikilidou [1], M. Yavropoulou [2], M. Antoniou [1], E. Papakonstantinou [1], A. Mousiolis [2], P. Chalkia [3], D. Pantelidou [3], A. Lasaridis [1], J. Yovos [2], P. Zebekakis [1]. *[1] Hypertension Excellence Center, 1st Department of Internal Medicine, AHEPA University Hospital, Thessaloniki, GREECE, [2] Division of Endocrinology and Metabolism, AHEPA University Hospital, Thessaloniki, GREECE, [3] Haemoglubinopathy Unit, 1st Department of Internal Medicine, AHEPA University Hospital, Thessaloniki, GREECE*

Objective: Sickle cell disease is a disease of microcirculation, although several theories also suggest involvement of large vessels. However, data on central aortic blood pressure (CBP) and arterial stiffness of subjects with sickle cell disease are conflicting. The aim of the present study was to assess CBP and arterial stiffness in adult patients with sickle cell disease compared with control subjects.

Design and method: 86 subjects were recruited 46 patients (male=15), and 36 healthy controls (male=18). Mean age of the population was 43.3±9.9 years for patients and 40.0±11.2 years for controls (p>0.05). Demographic characteristics and anthropometric characteristics were comparable in the two groups. Central aortic systolic and diastolic blood pressure (CSBP and CDBP), augmentation index (Aix), and pulse wave velocity (PWV), were measured in both groups with the Sphygmocor (Atcor Medical).

Results: Sickle cell disease patients showed significantly lower CDBP compared to controls (70.0±8.3 mmHg vs 80.4±9.7mmHg). Interestingly Aix was higher in the patient group (24.9±9.6% for patients vs 12.9 ± 11.4% for controls, p<0.001). CSBP, and PWV however showed no difference between the two groups.

Conclusions: Despite the fact that sickle cell patients have lower central blood pressure levels, the Aix, which is an indirect index of arterial stiffness was higher in these patients. Other mechanisms and not arterial stiffness are responsible for the relative hypotension of sickle cell patients. These mechanisms remain to be identified.

PP.08.17 PREHYPERTENSION AND ARTERIAL STIFFNESS

P. Pietri, C. Vlachopoulos, N. Ioakeimidis, M. Abdelrasoul, D. Terentes-Printzios, I. Gourgouli, C. Stefanadis. *Hypertension Unit, 1st Cardiology Department, Athens Medical School, Hippokration Hospital, Athens, GREECE*

Objective: Prehypertension or high normal blood pressure, defined either as systolic blood pressure (SBP) of 130-139 mmHg and/or diastolic blood pressure (DBP) of 85-89 mmHg has been associated with increased cardiovascular risk and incident hypertension. Although there was evidence for feasibility of treating prehypertension, recent guidelines do not recommend treatment of high normal BP, even in patients at high risk. The aim of the present study was to investigate the impact of prehypertension on arterial stiffness, a significant contributor in the pathophysiology of hypertension and an independent predictor of cardiovascular events.

Design and method: We studied 226 healthy individuals whom we divided into two groups according to the range of normal BP levels (1. subjects with high normal BP: SBP of 130-139 mmHg and/or DBP of 85-89 mmHg, N=137 and 2. subjects with normal BP: SBP of 120-129 mmHg or lower and/or DBP of 80-84 mmHg or lower, N=89).
Arterial stiffness was assessed by measuring carotid-femoral pulse wave velocity (PWV) using the Complior device.

Results: Subjects with prehypertension were older (48.7±15.6 vs 41.3±12.8 years), with higher body mass index (BMI) (27.1±3.9 vs 24.9±4.2 Kg/m²), higher levels of total cholesterol (204.6±38.1 vs 190.7±35.2 mg/dl) and triglycerides (101.8±49.0 vs 87.2±35.8 mg/dl) compared to individuals with normal BP. Pulse wave velocity was increased in prehypertensives compared to those with normal BP (6.64±1.22 vs 6.15±1.11 m/s, p<0.01). However, this difference became non-significant after adjustment for age, gender, smoking, BMI and total cholesterol (p=NS).

Conclusions: There is no evidence of harmful effect of prehypertension on arterial stiffness. Albeit our study population comprised of subjects with low cardiovascular risk, the present findings reinforce the notion that prehypertension is a clinical condition that warrants no pharmacological treatment.

PP.08.18 COMPARATIVE EFFECTS OF INDAPAMIDE SR AND HYDROCHLOROTHIAZIDE ON CENTRAL BLOOD PRESSURE AND ARTERIAL STIFFNESS IN HYPERTENSIVE PATIENTS: A RANDOMIZED TRIAL

E. Pavlova, Y. Kotovskaya, Z. Kobalava.
Peoples Friendship University of Russia, Moscow, RUSSIA

Objective: Differential effects of antihypertensive drugs on central blood pressure (BP) and arterial stiffness may have prognostic significance. The aim of the study was to compare indapamide SR and hydrochlorothiazide (HTZ) effects on central BP and arterial stiffness when added to monotherapy with ACE inhibitor (ACEi).

Design and method: 44 hypertensive patients (30 male, 55.2±3.2 years (M±SD) with clinical BP > 150/90 mmHg and daytime BP by ABPM > 135/85 mmHg after monotherapy with an ACEi for 6 weeks were randomized for adding indapamide SR 1,5 mg or HTZ 25 mg to treatment regimen. Measurement of clinic BP, central BP and pulse wave velocity (PWV) was done before and after 12 weeks after diuretic administration. Treatment-induced changes were considered significant if p<0,05.

Results: Treatment with both diuretics resulted in significant and similar decrease in clinic BP: in indapamide SR-treated subjects from 157±6/95±5 to 124±3/78±3 mmHg (p<0,05), HTZ-treated subjects from 158±7/94±5 to 126±4/80±3 mmHg (p<0,05). The decrease in central systolic BP was significant and similar as well: in indapamide SR-treated from 142±13 to 115±10 mmHg, -27±3,2 mmHg, in HTZ-treated from 141±13 to 118±12 mmHg, -22±4,8 mmHg. Decrease in central pulse pressure (PP) and augmentation index (AIx@75bpm) was significantly more evident in indapamide SR group than in HTZ group: for PP, respectively, from 53±10 to 37±7 mmHg, -16±4,0 mmHg and from 53±8 to 42±8 mmHg, -11±2,5 mmHg, p<0,05 compared to indapamide SR; for AIx@75bpm, respectively, from 28±7 to 22±5%, 6±2,0% and from 29±7 to 26±8%, -3±1,0%, p<0,05 compared to indapamide SR. PP amplification increased in indapamide SR-treated subjects and decreased in HTZ-treated ones: respectively from 119±8 to 124±9%, 5±2,7 mmHg, for HTZ from 120±10 to 112±7%, -8±3,1 mmHg, p<0,05 compared to indapamide SR. The decrease in PWV was similar and not significant: for indapamide SR from 11.7±6.5 to 9.6±6.0 m/s, for HTZ from 11.9±7.2 to 10.1±5.2 m/s.

Conclusions: Despite similar reduction in clinic brachial BP, indapamide SR 1,5 mg is more effective then HTZ 25 mg in terms of CBP reduction due to its impact on reflected wave characteristics.

PP.08.19 THORACIC AORTA REMODELING: CORRELATION WITH ARTERIAL STIFFNESS AND CARDIOVASCULAR ORGAN DAMAGE IN MILD HYPERTENSIVES

C. Mongiardi, A.M. Maresca, C. Marchesi, F. Annoni, L. Merletti, V. Vacirca, C. Gadaleta, A. Bertolini, L. Guasti, A.M. Grandi. *Università degli Studi dell'Insubria, Varese, ITALY*

Objective: In hypertensive patients thoracic aorta dilatation is a common phenomenon; it entails high risk of developing severe diseases such as aneurysm or dissection. Aim of the study was to evaluate in early stage of hypertensive disease aortic thoracic morphological parameters and their correlation with blood pressure (BP), aortic stiffness, carotid and cardiac organ damage.

Design and method: In this prospective study we enrolled 119 consecutive patients without cardiovascular disease or diabetes, not smokers: 78 were never treated mild hypertensive (mean 24h-BP>130 and/or 80mmHg), 41 were normotensive subjects matched for age, sex, body mass index and body surface area (BSA). For each subject we evaluated office and 24 hours BP. Each patient underwent arterial tonometry (central BP and pulse wave velocity, PWV), echocardiography and carotid ultrasonography.

Results: 24h-hours BP, central BP and PWV were higher in hypertensives (131±9/84±7 vs 115±6/74±4mmHg, p<0.001; 124±12 vs 115±15mmHg, p=0.013; 7.1±2 vs 6.2±1m/s, p=0.04). Aortic root and ascending aorta were normal in all subjects but higher in hypertensives (32.3±4vs30.7±4mm, p=0.04, 29.3±3.7 vs 27.7±3.3mm, p=0.01). Transverse aortic arch diameter was normal and similar in two groups. Root and ascending aorta diameters did not show significant correlation with office systolic and diastolic BP or 24-hours BP while these correlated with central systolic aortic pressure (r=0.315, p=0.001, r=329, p=0.001) and PWV (r=0.196, p=0.04, r=0.227, p=0.02). They also showed significant correlation with left ventricular mass (r=0.179, p=0.05, r=0.249, p=0.007) and relative wall thickness (r=0.291, p=0.001, r=0.347, p=0.001) but not with carotid intima-media thickness. Aortic arch diameter didn't show any correlation with aforementioned cardiac or vascular parameters.

Conclusions: In our study aortic parameters (root and ascending aorta diameters) resulted higher in mild hypertensives; these parameters correlated with cardiac but not carotid organ damage. Aortic remodeling was related with central blood pressure better than office and 24 hours blood pressure. Our findings suggest potential usefulness of central pressure measurement in early hypertensives stages to better predict aortic remodeling.

PP.08.20 INFLUENCE OF BISOPROLOL AND VERAPAMIL ON PERIPHERAL AND CENTRAL PRESSURE, LEFT VENTRICULAR DIASTOLIC FUNCTION AND ARTERIAL STIFFNESS OF HYPERTENSIVE PATIENTS

G. Mikhaylov [1], I. Orlova [2], F. Khezheva [1], M. Vitsenia [1], F. Ageev [1]. *[1] Russian Cardiology Research Center, Moscow, RUSSIA, [2] Moscow State University, Moscow, RUSSIA*

Objective: The aim of the study was to compare the effect of treatment β- blocker bisoprolol and calcium antagonist verapamil on peripheral and central pressure , left ventricular diastolic function (DFLV) and arterial stiffness of patients with hypertension.

Design and method: Included 60 patients (mean age 55 ± 12 years), 29 men, 31 women with hypertension I-IIst. and heart rate more 75 beat/min. Blood pressure, resting heart rate (HR), augmentation index (Alx %), systolic (cSBP) and pulse pressure (cPP) in the aorta, pulse wave velocity on carotid-femoral (PVWcf) and ankle - brachial (PWVab), DFLV were evaluatedat baseline and after 3 months of therapy with bisoprolol and verapamil.

Results: Both type of therapy significantly decreased SBP, DBP , PP, HR. Bisoprolol significantly decreased cSBP (from 142.7 to 136.6 mm Hg), cPP (from 49.7 to 43.3 mmHg); and Alx % was increased (from 31.5 to 35.2). Verapamil decreased cSBP significantly from 135.4 to 126.9 mm Hg. The changes of AIx% and cPP were not significant . DFLV dynamics were not found on both groups. PWVcf (-11.5 %) and PWVab (-7.5%)

were significantly decreased in the bisoprolol group. Bisoprolol showed antistiffening effect that was better than verapamil.

Conclusions: Both drugs showed a comparable reduction in the central and peripheral pressure, HR . In direct comparison with bisoprolol showed a more pronounced effect on surrogate prognosis marker PWV compared with verapamil.

PP.08.21 HIV INFECTION: ARTERIAL ALTERATION AND THEIR RELATIONSHIP WITH ANTIRETROVIRAL THERAPY

A. Maloberti [1], P. Villa [1], P. Meani [2], S. Nava [2], P. Campadello [2], M. Baroni [2], L. Frigerio [2], A. Gori [3], A. Bandera [3], F. Sabbatini [3], F. Cesana [2], C. Giannattasio [2].
[1] Department of Health Science, Milano-Bicocca University, Milan, ITALY, [2] Cardiologia IV, A. De Gasperis Dept. Niguarda Ca' Granda Hosp. and Milano-Bicocca University, Milan, ITALY, [3] Infectious Disease Department, San Gerardo Hospital, Monza, ITALY

Objective: Highly Active Anti Retroviral Therapy (HAART) has determined a dramatic change in the natural history of HIV infection causing an important decrease in infective cause of death. An increase in chronic comorbidities has been observed and both HAART and HIV infection itself has been advocate to be the cause. Aim of our study is to evaluate the arterial effects of HAART in HIV-infected subjects.

Design and method: We enrolled 55 HIV-infected subjects without known cardiovascular risk factors on HAART (group A; age 47.2±3.1years; female 16.3%; clinic BP 130/77±14.4/9.1mmHg), 34 healthy subjects served as control (group B; age 49±6.4years, female 17.6%; BP 126.2/77.6±7.3/5.5mmHg). Arterial stiffness was measured by aorto-femoral Pulse Wave Velocity and Pulse Wave Analysis (PWV and PWA, Sphygmocor) while carotid-IMT by a semi-automatic echotracking system (Esaote-WTS).

Results: For similar age and BP values group A shown an higher PWV (10±1.7 vs 9.4±1.1 for group A and B respectively; p=0.038) and Augmentation Index (22.9±12 vs 17.1±.9.8 for group A and B respectively; p=0.018) while IMT was superimposable between group (551.4±111.6 vs 568.2±95.1 for group A and B respectively; p=ns). No correlation was seen between HAART (time on HAART and specific drugs) and chronic viral infection (time of infection, CD4, CD4 nadir and HIV-RNA) whit arterial parameter.

Conclusions: HIV subjects on ART shown an higher arterial stiffness when compared to an age and BP superimposable healthy group. HAART related arterial alterations can leads to the observed increase in cardiovascular events.

PP.08.22 ACUTE EFFECT OF DIALYSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE ON ARTERIAL FUNCTION

J. Lopez-Rivera [1], P. Loyo [2], A. Andrade [3], S. Pereira [1], W. Zerpa [1].
[1] V Departamento, Unidad de Hipertension Arterial, Hospital Jose Ma Vargas, San Cristobal, VENEZUELA, [2] Servicio de Nefrología, Hospital Jose Ma Vargas, San Cristobal, VENEZUELA, [3] Organizacion Nacional de Transplante, ONTV, San Cristobal, VENEZUELA

Objective: The aim is evaluate the effect on vascular function, capacitive arterial compliance/large artery elasticity (C1) and oscillatory reflective compliance/small artery elasticity (C2) in acute dialysis on patients with chronic kidney dissease

Design and method: An observational cohort study , patients with chronic kidney diseasse on dialysis, to assesses changes in peripheral hemodinamics and vascular function C1,C2 and peripheral vascular resistance, using the HDI/Pulse Wave CR 2000, before and after dialisys.

Results: Twenty five patients with chronic kidney dissease were evaluated in a dialysis program, all of them more tan one year in the program, 13 women, 12 male, averege age 54 years, the prevalent etiology was arterial hypertension and diabetes in a 86% both.

Brachial pressure (BP), Pulse pressure(PP), Capacitive arterial compliance /large artery elasticity(C1),oscillatory/reflective compliance /small artery elasticity(C2), pre and post dyalisis . Hospital Central de San Cristóbal y UNETACA Táchira, 2012.

Parameter	Media	Standar desviation	Standar Error	95% Confidence interval		Significance test		
				upper	lower	t	gl	Sig. (bilateral)
BSP b – BSP a	- 3,59	23,54	5,71	-15,69	8,51	0,629	16	0,539
BDP b – BDP a	0,26	12,41	3,01	-6,12	6,64	0,086	16	0,933
PP b – PP a	2,59	9,42	2,38	-2,26	7,43	1,133	16	0,274
C1 b – C1 a	0,76	3,79	0,92	-1,19	2,72	0,831	16	0,418
C2 b – C2 a	0,02	1,51	0,37	-0,75	0,80	0,064	16	0,949

Note: (b) before - dyalisis, (a) after - dyalisis

Conclusions: Statistically significant changes after dialysis were observed in a components of diastolic blood pressure and small artery elasticity (C2). Not in systolic blood pressure or large artery elasticity (C1).Although effective dialysis by the KTv measurement. Dialysis improve endothelial function observed by C2 changes.

PP.08.23 PARAMETERS OF ARTERIAL STIFFNESS IN NORMOTENSIVE PATIENTS WITH VISCERAL OBESITY

M. Druzhilov, V. Korneva, T. Kuznetsova
Petrozavodsk State University, Petrozavodsk, RUSSIA

Objective: Visceral obesity (VO) is a factor of vascular remodeling and increased arterial stiffness (AS). At the same time, body mass index (BMI) and waist circumference (WC) reflect primarily metabolically neutral subcutaneous fat. The comparative analysis of AS parameters in normotensive patients with VO was held.

Design and method: 163 normotensive patients without cardiovascular disease were examined (mean age 45,0±5,4, 74,8% male), 81,0% with abdominal obesity (AO), 49,7% obese (BMI >=30 kg/m2). VO was diagnosed by ultrasound epicardial fat thickness (EFT) when it was equal to or exceeded 75 percentile value. Among patients with 31-45 years old it was 4,8 mm in AO patients, 3,5 mm without AO, 46-55 years old - 5,8 mm and 4,4 mm respectively. Blood lipid, glucose profiles, uric acid, creatinine and fibrinogen levels were estimated, bifunctional ambulatory blood pressure (BP) monitoring was performed using the portable recorder BP Lab®. The following AS parameters were assessed: average aortic daily pulse wave velocity (PWVao), augmentation index (Aix), average aortic daily systolic blood pressure (SBPao). Statistical analysis was conducted with t-test and multivariate linear regression analysis.

Results: VO was diagnosed in 28,8%. In patients with VO higher values of PWVao (7,9±0,7 m/s vs 7,5±0,5 m/s, p<0,001), Aix (-28,0±19,8% vs -40,3±16,5%, p<0,001) and SBPao (109,7±5,6 mm Hg vs 107,2±5,0 mm Hg, p<0,001) were found. Significant differences in other parameters were not found: average WC was 100,9±10,6 cm vs 100,1±8,4 cm, BMI - 30,9±4,7 kg/m2 vs 29,7±3,5 kg/m2, average daily BP levels - 118,7±6,4/74,0±4,0 mm Hg vs 117,5±6,1/72,5±4,1 mm Hg. More large values of AS parameters were in the group with VO in comparison with AO patients: 7,9±0,7 m/s vs 7,6±0,6 m/s (p<0,001), -28,0±19,8% vs -36,3±18,6% (p<0,001) and 109,7±5,3 mm Hg vs 108,4±5,1 mm Hg (p<0,001) respectively. The multivariate linear regression analysis was used for pre-dictive estimate of PWVao. The following regression equation was obtained: age*0,021+fasting blood glucose*0,134+EFT*0,139+SBP*0,023+ DBP*0,036. For this regression model the determination coefficient was 0.9.

Conclusions: Higher AS parameters were found in patients with VO diagnosed by measuring EFT. PWVao value was mainly depended from the age, BP, fasting blood glucose levels and EFT.

PP.08.24 COMPARISON OF AMBULATORY CENTRAL AND PERIPHERAL BLOOD PRESSURE BETWEEN THE SECOND AND THIRD DAY OF THE LONG INTERDIALYTIC INTERVAL IN HEMODIALYSIS PATIENTS

G. Koutroumpas [1], P. Sarafidis [2], P. Georgianos [2], A. Karpetas [2], A. Protogerou [3], P. Malindretos [1], C. Syrganis [1], S. Panagoutsos [4], P. Pasadakis [4]. *[1] Department of Nephrology, Achillopouleion General Hospital, Volos, GREECE, [2] Medical School, Aristoteleion University, Thessaloniki, GREECE, [3] Hypertension Unit and Cardiovascular Research Laboratory, Laiko Hospital, Medical School, National and Kapodistrian Univ. Athens, GREECE, [4] Department of Nephrology, Alexandroupolis University Hospital, Alexandroupolis, GREECE*

Objective: The conventional thrice-weekly hemodialysis schedule includes two regular (about 2 days) and one long (about 3 days) interdialytic interval periods. During the long interval patients have to deal with a larger amount of metabolic products and volume accumulation and recent data suggest that the end of the 3-day period associates with the highest cardiovascular risk. This study compared for the first time ambulatory central blood pressure between Day 2 and Day 3 of a long interdialytic interval.

Design and method: Thirty-two end-stage renal disease patients receiving conventional hemodialysis (mean age 64.3±14 years and median time on renal replacement therapy 37.6 months) were included in the study. All underwent a 72-hour Ambulatory Blood Pressure Monitoring covering the large interdialytic interval, with the novel Mobil-O-Graph device (IEM, Stolberg, Germany). Mobil-O-Graph is a validated brachial cuff-based automatic oscillometric device that records brachial BP and pulse waveforms and calculates central BP through mathematical transformation. Daytime and night-time ambulatory BPs of Day 3 vs Day 2 were compared.

Results: Ambulatory central aortic SBP and DBP on Day 3 were significantly higher than on Day 2 (daytime, 124.3±17.8 vs 118.03±17.7 and 81.8±10.9 vs 77.4±11.3 mmHg, p<0.001; night-time 126.1±21.8 vs 120.26±23.1 and 80.8±14.5 vs 76.5±12.8 mmHg, p<0.001, respectively). Ambulatory brachial SBP and DBP followed the same pattern (daytime 136±22.1 vs 129.36±21.7

and 80.2±10.8 vs 75.5±11 mmHg, p<0.001; night-time 138.5±26.3 vs 131.4±26.4 and 79.4±13.7 vs 74.8±12.5 mmHg, p<0.001, respectively,). Central and peripheral pulse pressures were also significantly higher in Day 3 vs Day 2 and heart rate significantly lower, during daytime but not during night-time. Fourteen patients needed increase at their antihypertensive drugs specifically for Day 3.

Conclusions: This is the first study evaluating central BP during a 72-hour interval in hemodialysis patients. The significant increase in central BP during Day 3 follows the same pattern with that of peripheral BP and may be a major mechanism of elevated cardiovascular risk at the final hours of the week in this population.

PP.08.25 ASSOCIATION OF ARTERIAL STIFFNESS AND GLOMERULAR FILTRATION RATE IN UNTREATED HYPERTENSIVE PATIENTS WITHOUT CHRONIC KIDNEY DISEASE

Y. Kotovskaya, S. Villevalde, Z. Kobalava
Peoples Friendship University of Russia, Moscow, RUSSIA

Objective: The relationship between arterial stiffness and kidney function in middle-aged patients with uncomplicated hypertension is not well studied. Accordingly the aim of the study was to investigate the association between estimated glomerular filtration rate (eGFR) and arterial stiffness in middle-aged patients with untreated arterial hypertension.

Design and method: A cross-sectional study included 101 non-diabetic patients (age 53,5±12,3 years, 48,5% males) with untreated arterial hypertension without target organ damage on routine examination with estimated glomerular filtration rate by CKD-EPI formula (eGFR) >60 ml/min/1,73m2 and albumin/creatinine ratio<30mg/g in a morning urinary spot. Arterial stiffness was evaluated by central pulse wave analysis and and pulse wave velocity measurement (SphygmoCOr, AtCor, Australia). Linear regression analyses were used to assess the cross-sectional associations between arterial stiffness parameters and eGFR. A two-sided p-value of < 0.05 was regarded as significant.

Results: PWV >12 m/s was found in 54 (53,5%) patients. In multivariate analysis decrease of eGFR<90,6 ml/min/1,73m² was a strong independent predictor (χ^2=7,6, p<0,01) of increased arterial stiffness along with metabolic risk factors and abdominal obesity. Arterial stiffness was assessed by eGFR quartiles: I > 94 ml/min/1,73m² , II 91-94 ml/min/1,73m², III 79-91 ml/min/1,73m² , IV 61-79 ml/min/1,73m². There was a progressive increase from I to IV quartile of PWV (9,9±3,8, 11,5±2,6, 12,6±3,3 (p<0,05 compared to I quartile), 12,7±2,5 (p<0,05 compared to I quartile) m/s), augmentation index@75 bpm (AIx) 14,8±13,5%, 24,9±10,5%, 26,3±13,0% (p<0,05 compared to I quartile), 31,5±5,9% (p<0,05 compared to I quartile). Central systolic BP, AIx and PWV were significant independent predictors of eGFR: respectively, β= -0,47, p<0,01, β= -6,2, p<0,01, β= -2,33, p<0,01.

Conclusions: There is strong association between increased arterial stiffness assessed by direct and indirect measures and decrease in eGFR in hypertensive subjects with normal kidney function.

PP.08.26 TEN-YEAR TENDENCY OF PULSE WAVE VELOCITY IN JAPANESE MEDICAL STUDENTS

T. Kita, K. Kitamura. *Circulatory and Body Fluid Regulation, Dept. Internal Medicine, Faculty of Medicine, University of Miyazaki, Miyazaki, JAPAN*

Objective: Atherosclerosis of the artery begins very early phase of life. Environmental factors have strong impact for the progression of atherosclerosis, and thus recent rise in health awareness may bring good influence for the condition of arteries. To investigate this expectation, we measured pulse wave velocity (PWV), a marker for arterial stiffness, on fifth year of medical student for ten years. Well matched backgrounds of the subjects will be advantageous for investigation of the tendency.

Design and method: PWV was measured using an automatic waveform analyzer (form PWV/ABI, BP-203RPE; Omron Colin, Tokyo, Japan). The measurement was curried in outpatient office of University of Miyazaki Hospital at 13:30 to 14:30 while small group of the students were attending clinical training. The outpatient office is well controlled in comfortable condition throughout the year.

Results: We measured 915 of the students (male 517, 24.9 ± 3.2 years old). Average blood pressure (BP) was 119.8 ± 12.5/67.4 ± 8.4 mmHg, and average PWV was 1152.8 ± 149.1 cm/sec. PWV was significantly correlated with systolic and diastolic BP, pulse rate and age as expected. PWV was significantly higher in male than female (1197.8 ± 152.0 vs. 1094.3 ± 122.7, p<0.0001), so gender specific analysis was done for annual changes of PWV. PWV in male students had a tendency to decrease and there was significant decrease of PWV (p < 0.05) between starting year (2003) and last two years (2011-12). On the other hand, there was no change in PWV of female students. Also, there were no changes of the BP in both genders.
Conclusions: Preferable decrease of the stiffness of artery in young male was observed in Japanese medical student.

PP.08.27 CAROTID ATHEROSCLEROTIC PLAQUES ASSOCIATED WITH ARTERIAL STIFFNESS

G. Kim, J. Kim, K. Moon, K. Yoo, C. Kim.
St. Vincents Hospital, Suwon, SOUTH KOREA

Objective: Atherosclerotic plaques of carotid arteries increase the risk of cerebrovascular events. Arterial stiffness strongly associates with the development of atherosclerosis. This study aimed to elucidate the association between carotid atherosclerotic plaque and arterial stiffness at different arterial site.

Design and method: One hundred thirty-three subjects (M:F=62:71, mean age=54.4±11.7 years), among subjects who received carotid ultrasonography, the brachial-ankle pulse wave velocity (baPWV) and non-invasively semi-automated radial artery applanation tonometry (using Omron HEM-9000AI) in the Department of Internal Medicine, St. Vincent's Hospital, from July 2011 to February 2013 were enrolled in this study. Pulsatile stress (PS) was calculated as the product of heart rate and brachial PP.

Results: Sixty-seven subjects (mean age=58.2±10.1 years) had atherosclerotic plaques of carotid arteries. There were significant differences in age (odds ratio 1.076, 95% CI 1.038-1.116, p<0.0001), pulse pressure (odds ratio 1.055, 95% CI 1.019-1.092, p=0.003), PS (odds ratio 1.011, 95% CI 1.011-1.081, p=0.005), baPWV (odds ratio 1.044, 95% CI 1.002-1.006, p<0.0001), intima-media thickness (odds ratio 1.029, 95% CI 1.011-1.082, p=0.001) between subject without and with atherosclerotic plaques of carotid arteries. In multivariate analysis, baPWV (odds ratio 1.211, 95% CI 1.001-1.005, p=0.034) and PS (odds ratio 1.001, 95% CI 1.001-1.002, p=0.033) were associated with atherosclerotic plaques. maximum IMT was significantly correlated with age (r=0.382, p<0.0001), brachial PP (r=0.281, p=0.001), brachial PS (r=0.181, p=0.038), SBP2 (r=0.202, p=0.021), central PP (r=0.321, p<0.0001), central PS (r=0.302, p<0.0001), RaAIx (r=0.235, p=0.007). Mean IMT was significantly correlated with age (r=0.433, p<0.0001), systolic BP (r=0.256, p=0.003), brachial PP (r=0.369, p<0.0001), brachial PS (r=0.265, p=0.002), SBP2 (r=0.248, p=0.004), central PP (r=0.357, p<0.0001), central PS (r=0.351, p<0.0001), RaAIx (r=0.209, p=0.016).
In multivariate analysis, baPWV (odds ratio 1.211, 95% CI 1.001-1.005, p=0.034) and PS (odds ratio 1.001, 95% CI 1.001-1.002, p=0.033) were associated with atherosclerotic plaques. However, central hemodynamics was not correlated with atherosclerotic plaques.

Conclusions: We found that atherosclerotic change of vascular wall may be more affected by chronically increased pulsatile stress and baPWV. Therefore, it is suggested that atherosclerotic change of carotid artery may be influence on various parameters of arterial stiffness at different site of arterial tree.

PP.08.28 EFFECT OF HYPERBARIC OXYGENATION ON EPOXYGENASE PROTEIN EXPRESSION IN AORTA OF HEALTHY AND DIABETIC RATS

A. Kibel , I. Drenjancevic. *University J.J. Strossmayer in Osijek, School of Medicine Osijek, Department of Physiology and Immunology, Osijek, CROATIA*

Objective: In previous studies, we found that hyperbaric oxygenation (HBO) influences vascular reactivity, possibly through upregulation of epoxyeicosatrienoic acids (EETs). EETs, produced by specific epoxygenase enzymes, have a protective role in many conditions including atherosclerosis and hypertension. Impairment of this role of EETs contributes to endothelial dysfunction in hypertension and increase in EETs production attenuates abnormal renal function. Infusion of EETs decreases mean arterial pressure (MAP) in rats. The aim in this study was to evaluate the effect of HBO on epoxygenase protein expression and blood pressure in healthy or streptozocin-induced diabetic male Sprague-Dawley rats.

Design and method: Rats were divided into control and HBO groups. The HBO group was exposed to 100%O2 for 2 hours (with additional 15 minutes for compression/decompression) daily for 4 consecutive days. On the fifth day, anesthetized animals were sacrificed and aorta samples stored at -80ºC. Western blot analysis was performed with specific antibodies for rat epoxygenases (cytochrome P450 isoforms CYP2J3 and CYP2C11). Epoxygenase expression was quantified relatively to ß-actin expression. MAP was measured in separate anesthethized control and HBO animals after insertion of a femoral artery catheter. T-test or Mann Whitney U test was used to compare HBO and control values, depending on distribution normality.

Results: Relative CYP2J3/ß-actin expression was similar between the HBO and control group both in healthy (1.488±1.840 [n=11] vs.1.160±0.785 [n=9]) and in diabetic (1.119±0.495 [n=9] vs. 0.945±0.506 [n=11]) rats. Relative CYP2C11/ß-actin expression was similar between healthy HBO and control animals (1.295±1.031 [n=9] vs.1.425±1.174 [n=8]), but it was statistically significantly higher in the HBO group of diabetic rats compared to control (1.395±0.448 [n=7] vs. 0.796±0.534 [n=7]; P<0.05, t-test). The used HBO protocol did not significantly alter MAP in either healthy (118.9±8.4 HBO [n = 6] vs. 113.0±3.4 mmHg control [n=6]) or diabetic (105.9±4.7 HBO [n=6] vs. 102.3±5.0 mmHg control [n=6]) rats.

Conclusions: The significant upregulation of CYP2C11 protein expression in diabetic rats by HBO suggests that upregulation of EETs production might partially explain beneficial vascular effects of HBO in diabetic subjects. However, direct alteration of MAP with this HBO protocol was not observed.

PP.08.29 SEX DIFFERENCE IN CHANGES OF ARTERIAL STIFFNESS INDEXES AFTER ISOMETRIC HANDGRIP EXERCISE

S. Joo, H. Choi, S. Kim, K. Kim
Jeju National University Hospital, Jeju, SOUTH KOREA

Objective: It has been shown that arterial stiffness is greater in women than men, especially after menopause. This study aimed to investigate the sex difference in dynamic changes of hemodynamic parameters and arterial stiffness indexes after isometric handgrip exercise.

Design and method: Thirty one subjects (14 postmenopausal women and 17 men) who underwent coronary angiography (CAG) were enrolled. After CAG, baseline arterial waveforms were traced at the aortic root and common iliac artery using right coronary catheters. Arterial waveforms were recorded at the same locations 3 min after the isometric handgrip exercise at 30~40% of the maximal handgrip power. Augmentation pressure (AP) and augmentation index (AI) were measured at the central aortic waveforms. Pulse wave velocity (PWV) was calculated using the ECG-gated time difference of the upstroke of the arterial waveforms and the distance between the aortic root and the common iliac artery.

Results: Age (W 66.9±9.0 vs. M 65.2±5.9 years), prevalence of hypertension, coronary artery disease, diabetes or hyperlipidemia, and medications were not different significantly between women and men. Baseline central pulse pressure (PP) was greater in women (W 65.7±16.9 vs. M 51.9±15.3 mmHg), but central systolic BP (SBP), AP, AI, and PWV were not significantly different. After handgrip exercise, central SBP, central PP, and AP increased in both women and men. AI did not changed, but delta-AI after exercise tended to be greater in men (W 1.27±3.96 vs. M 3.37±7.11%) without statistical significance. PWV inclined only in men, and delta-PWV after exercise was greater in men (W 0.24±1.08 vs. M 1.31±1.56 m/sec, p<0.05).

Conclusions: Compared to women, men showed greater changes of arterial stiffness indexes after isometric handgrip exercise although baseline central PP was lower.

	Women (n=14)		Men (n=17)	
	Baseline	Exercise 3 min	Baseline	Exercise 3 min
Heart rate (/min)	62.3±8.0	69.6±14.3*	64.5±10.5	69.5±10.6*
Central SBP (mmHg)	127.8±20.9	150.6±26.1*	116.5±18.6	136.4±19.4*
Central PP (mmHg)	65.7±16.9†	79.1±18.0*†	51.9±15.3	63.5±16.0*
Augmentation P (mmHg)	11.9±7.1	15.2±8.5*	9.5±6.5	13.8±10.2*
Augmentation index (%)	18.7±11.2	19.9±11.7	17.8±11.4	21.2±13.1
Peripheral SBP (mmHg)	134.9±19.1	149.5±26.9*	122.9±18.5	140.7±22.9*
Peripheral PP (mmHg)	73.5±16.7	87.1±21.3*	60.1±16.4	73.1±18.7*
PWV (m/sec)	10.47±1.63	10.72±1.92	10.36±1.79	11.67±2.45*

* p<0.01 vs. baseline, †p<0.05 vs. men
SBP; systolic blood pressure, PP; pulse pressure, PWV; pulse wave velocity

PP.08.30 BLOOD PRESSURE AMPLIFICATION IN RELATION TO PLASMA ADVANCED GLYCATION END PRODUCTS IN A CHINESE POPULATION

Q. Huang, Y. Li, C. Sheng, L. Li, J. Wang
Shanghai Institute of Hypertension, Shanghai, CHINA

Objective: Accumulation of advanced glycation end products (AGEs) in the human body might engender arterial stiffening. We investigated the association of plasma AGE concentration with blood pressure amplification in a Chinese population.

Design and method: The study subjects were recruited from a newly established residential area in the suburb of Shanghai in 2009. Using the SphygmoCor system, we recorded arterial waveforms. The central-to-brachial amplification was expressed as the systolic pressure difference (SPD), the pulse pressure difference (PPD), and the pulse pressure ratio (PPR). Plasma AGE concentration was measured by the ELISA method and logarithmically transformed for statistical analysis.

Results: The 1051 study participants (mean age 55.1±13.1 years) included 663 (63.1%) women, 390 (37.1%) hypertensive patients and 90 (8.6%) diabetic or prediabetic subjects. Men, compared with women, had higher plasma AGE concentration (5.62 vs. 5.07 µg/mL, P=0.02) and greater (P<0.0001) SPD (11.8 vs. 9.3 mmHg), PPD (13.0 vs. 10.5 mmHg) and PPR (133.9 vs. 126.6 %). Multiple regression analyses demonstrated that plasma AGEs concentration was significantly and negatively associated with PPR (-2.39% decrease per 10-time increase in plasma AGEs concentration, P=0.03) but not with SPD and PPD (P= 0.11 and 0.13, respectively). This association between plasma AGEs concentration and PPR became more prominent in men (-5.17%, P=0.01) and in the presence of at least one of the following three cardiovascular risk factors, overweight and obesity, diabetes and prediabetes or current smoking (-4.42%, P=0.006).

Conclusions: Plasma AGEs are associated with pulse pressure amplification as assessed by PPR, especially in men and in the presence of several common cardiovascular risk factors.

PP.08.31 BUCKBERG INDEX ASSOCIATES WITH VASCULAR DAMAGE IN A COHORT OF HYPERTENSIVE MALES

A. Hermida, J.E. López, A. Pascual, V. Martínez, G. Calvo, I. Rodríguez, C. Calvo. *Hypertension Unit, Clinic Hospital, Santiago de Compostela, SPAIN*

Objective: Pulse wave analysis by applanation tonometry let us know by a non-invasive way, three different indexes of cardiovascular function: Augmentation index, ejection duration and subendocardial viability ratio (the Buckberg index, BI). When myocardial perfusión decreases and cardiac ischaemia appears, then BI falls under 50%.
The main objective les to assess relationship between BI and other different vascular damage markers in a cohort of male hypertensive subjects.

Design and method: A cross-sectional study was conducted in hypertensive males. 48-hour BP monitoring was performed using a validated device (Spacelabs 90207).
All subjects underwent radial artery pulse wave analysis by applanation tonometry with SphygmoCor Px®, Vx®, to obtain BI.
To assess vascular damage markers, following examinations were held: carotid artery ultrasound with intima/media thickness (IMT), carotid femoral PWV by Sphygmocor At Cor® and oscillometric measurement of ABI.

Results: A total of 256 hypertensive males were enrolled in the study (mean age: 54.4 years). Buckberg index was categorized by quartiles; 1st Q: < 126% (n: 44); 2nd Q: 126-146% (n: 62); 3rd Q: 146-166% (n: 61) and 4th Q: > 166%(n:89).
Those hypertensive males in the 1st Q, were elder (mean age: 62.25 years), lower dyastolic 48-hour BP, lower nocturnal blood pressure falling, higher heart rate, lower ABI and higher PWV compared to patients in the other quartiles. There were no differences regarding weight, waist circumference, body mass index, systolic 48-hour BP or IMT.

Conclusions: These data suggest that the subendocardial viability rate (Buckberg index) measured by applanation tonometry keeps relationship with other myocardial perfusion markers as heart rate or dyastolic blood pressure.
Those subjects with low BI are in a higher risk of increased arterial stiffness (higher PWV) and peripheral vascular damage (lower ABI). Thus, non invasive assessing of BI may help us to identify those hypertensive subjects with vascular disease.

PP.08.32 EFFECT OF GASOTRANSMITTERS ON THE CONTRACTILE ACTIVITY OF VASCULAR SMOOTH MUSCLES DURING HYPOXIA AND REOXYGENATION

S. Gusakova [1], Y. Birulina [1], I. Kovalev [1], A. Marchenko [1], L. Smagliy [1], M. Medvedev [1], S. Orlov [2]. [1] *Siberian State Medical University, Tomsk, RUSSIA,* [2] *University of Montreal Research Centre, Montreal, CANADA*

Objective: Hypoxia followed by reoxygenation causes damage not only cells of parenchymal organs, but primarily vascular cells, which leads to disruption their contractile function. Today is a very urgent problem of detail mechanisms and find ways to correct the hypoxic conditions. Great expectations associated with the role played gasotransmitters in regulation of contractile activity of smooth muscle in hypoxia and subsequent reoxygenation.
The study was aimed to elucidate (i) the ionic mechanisms of action of CO and H2S in contractile activity of vascular smooth muscle cells (VSMC) and (ii) the molecular interactions in the gaseous signaling system during hypoxia and reoxygenation.

Design and method: We used mechanography of the isolated endothelium-denuded rat thoracic aortic rings. The effects of H2S and CO donors (NaHS and CORM2, respectively) on VSMC contractions induced by membrane depolarization in high-K+ (30 mM KCl) solution and Phenylephrine were studied.

Results: Hypoxia causes a decrease in the contractile responses of vascular smooth muscle cells such as the action of a high potassium solution, and under the action of Phenylephrine.

Relaxing effect of hypoxia is mediated through increased potassium conductance of the membrane. During hypoxia reduced relaxing effects gasotransmitters CO and H2S.
Reoxygenation smooth muscle cells leads to a decrease in the contractile responses to high potassium solution and Phenylephrine, and also increases CO relaxing action on the contraction induced by Phenylephrine.

Conclusions: These data may indicate that for reoxygenation, presumably due to free radical flash molecular chain starts cellular events involved in the mechanism of carbon monoxide action relaxing receptacle. This molecular cascade includes the soluble guanylate cyclase and the Ca2 + - activated potassium channels of high conductivity.

PP.08.33 AUGMENTATION INDEX AND AORTIC STIFFNESS IN PATIENTS WITH ASCENDING AORTIC ANEURYSM

N. Gavriliuk, T. Druzhkova, O. Moiseeva, E. Moguchaya, M. Boyarinova, D. Krivonosov, O. Rotar, O. Irtyuga. *Federal Almazov Medical Research Centre, Saint-Petersburg, RUSSIA*

Objective: The aim of the study was to compare aortic stiffness in thoracic aortic aneurysm (TAA) development in patients with with bicuspid (BAV) and tricuspid (TAV) valve.

	TAV M ± σ	BAV M ± σ	Control M ± σ
BMI, kg/m²	29,4 ± 3,9	28,2 ± 6,0	29,6 ± 5,3
Smokers, n (%)	27(50)	13(68)	29 (58)
HN, n (%)	48 (89)	15 (71)	38 (76)
Diabetes, n (%)	13(24)	5(24)	20(40)***
Office SBP, mm Hg	137 ± 18	138 ± 36	133 ± 27
Office DBP, mm Hg	82 ± 11*	80 ± 15*	75 ± 11
Aortic diameter in the sinuses of Valsalva	43,6 ± 4,7	41,1 ± 6,0	33,8 ± 4,0**
Index of Sinuses of Valsalva	21,2 ± 2,6	21,2 ± 2,9	17,3 ± 2,1**
Aortic diameter in the sinotubular junction, mm	46,6 ± 4,7	45,6 ± 8,4	33,3 ± 3,3**
Max aorta	48,0 ± 3,6	46,3 ± 7,7	34,3 ± 3,6**
Augmentation	23 ±10	30 ±10**	22 ±10
Period of blood	33,6 ± 3,4*	34,9 ± 3,5**	32,0 ± 3,8
PWV, m\sec	8,0 ±1,8	6,7 ±1,4*	7,9 ±1,9

〈 - p < 0,05; ** - p < 0,001: *** p<0,0001 compared control group

Design and method: 75 pts with TAA: 21pts with BAV (mean age 52.8 ± 1.9 yrs; m:f=15:6), 54 pts with TAV (mean age 60.3± 0.8 yrs; m:f=39:15), and 50 pts with risk factors and without aorta pathology as control group (mean age 58.3 ± 0.8yrs; :1, m:f=35:15) were examined. Arterial stiffness was assessed by SphygmoCor device (Australia) using indirect carotid-femoral distance. The normal value of pulse wave velocity (PWV) was considered below 10 m/s. All pts were assessed at baseline and after 12 month.

Results: Pts with BAV and TAV were comparable in maximal and mean aortic diameter. We found no differences in pulse blood pressure in groups (55 ± 14 mm Hg in pts with TAV, 58 ± 36 mm Hg in pts with BAV, 58 ± 22 mm Hg in control group). Office diastolic BP was increased in pts with TAV as compared with control group (82 ± 11 versus 75 ± 11, p<0.01). Pulse wave velocity was lower, but augmentation index were higher in BAV pts than in the control and TAV group. There was increased period of blood ejection out in pts with BAV, that, probably, due to hemodynamic and morphologic characteristics of the valve.

Conclusions: Patients with BAV have changes in arterial vawe reflection, which could not be explained by young age only and likely due to properties of aortic wall. This features can play role in ascending aortic aneurysm formation in this subjects.

PP.08.34 BENEFICIAL EFFECT OF STENTING AND MULTIFACTORIAL DRUG THERAPY ON ARTERIAL STIFFNES IN ATHEROSCLEROTIC RENOVASCULAR HYPERTENSION

L. Fodor, M. Laganovic, V. Premuzic, D. Perkov, V. Ivkovic, T. Zeljkovic-Vrkic [1], M. Fistrek-Prlic [1], J. Kos [1], Z. Dika [1], B. Jelakovic [1]. *Department for Nephrology, Hypertension, Dialysis and Transplantation, University Hospital Zagreb, School of Medicine, U, Zagreb, CROATIA*

Objective: Patients with atherosclerotic renovascular hypertension (aRVH) have higher arterial stiffness (AS) than patients with other cardiovascular related diseases. It is still unresolved whether therapeutic strategies that are effective in reducing brachial blood pressure (BP) in patients with aRVH independently affects AS and central BP thereby influencing outcome. Our aim was to determine effect of stenting in addition to multifactorial drug therapy on markers of AS and clinical course in aRVH.

Design and method: In this longitudinal study we have enrolled 37 patients with unilateral aRVH. BP and indices of AS were determining at baseline, after 6 and 36 months. Average follow up period was 39 (21-46) months. Markers of AS were determined using Arteriograph, SpaceLabs was used for ABPM and Omron device for office BP measurements. After revascularization all patients received telmisartan 80 mg in addition to other antihypertensive drugs and statin.

Results: Baseline pulse wave velocity (PWV) was higher in aRVH patients (12.7m/s) compared to other high risk hypertensive patients. Three patients who deceased had the highest PWV (15.03m/s). At the end of follow up 31/34 improved BP valuesm, none was cured. Kidney function was unchanged in 23/34 patients, and deterioration was observed in 6 patients. After 6 months brachial BP was significantly lower and remained the same till the end of follow up period. Aortic augmentation index (AIx) significantly improved after 6 months (35.91(14.47) vs.32.18(10.42);p=0.03) and was unchanged after 3 years (39.65(10.54);p=0.55). PWV did not change after 6 months (12.7 (2.6) vs.13.7(3.1);p=0.13) but was significantly lower at the end of follow up (11.18(2.35);p=0.027).

Conclusions: Therapy based on stenting and multifactorial drug therapy reduces AS in patients with aRVH. AIx improved after 6 months what could be attributed to the usage of renin-angiotensin blockers. We failed to detect decrease of PWV after 6 months. Progressive reduction in PWV over time have been observed with no further fall in brachial BP and AIx what is in line with other studies .Combination therapy has beneficial effect on AS in patients with aRVH.Larger studies are needed to confirm predictive ability over and above brachial BP.

PP.08.35 REFERENCE VALUES FOR PULSE WAVE VELOCITY MEASURED BY AN OSCILLOMETRIC METHOD IN A POPULATIONAL SURVEY. DATA FROM SEPHAR II STUDY

R. Darabont [1], O. Tautu [2], A. Deaconu [2], I. Comanescu [2], S. Onciul [2], B. Dragoescu [2], D. Radu [2], M. Dorobantu [2]. *[1] University Emergency Hospital, Bucharest, ROMANIA, [2] Emergency Clinic Hospital, Bucharest, ROMANIA*

Objective: Our objective was to find out the reference values for pulse wave velocity (PWV) measured by a simplified and time-saving oscillometric method on a populational level during SEPHAR II study, the second national representative survey on hypertension prevalence in Romania.

Design and method: Following a selection based on the multi-stratified proportional sampling procedure, a number of 1975 subjects, who gave informed consent, were evaluated by means of a questionnaire, anthropometric, blood pressure (BP), 12 lead ECGs recordings, blood and urine analysis. PWV was measured with Arteriograph (TensioMed Ltd., Budapest, Hungary) in only 1104 of cases. After exclusion of subjects with diabetes, treated hypertension or dyslipidemia and overt cardiovascular disease the linear regression analysis (stepwise method) was applied to examine the influence of cardiovascular risk factors on PWV for 731 subjects (mean age 40.18±12.66 years, 51.8% females).

Results: PWV proved to be independent of gender, smoking and untreated lipid disorders, after adjustement for age and mean BP. Consequently, the reference values for PWV were established according to age and BP, the main determi-

nants of arterial stiffness (Table 1). This results were found similar (p>0.05) to those reported by The Reference Values for Arterial Stiffness' Collaboration based on stated methods, confirming previously good correlations between assessement of PWV with the Arteriograph and the values obtained using the SphygmoCor and the Complior devices.

Table 1: Pulsed wave velocity distribution by age and BP values

Age group (years)	Normal BP	High normal BP	Grade I HT	Grade II/III HT
< 30	7.18 ± 1.45	7.21 ± 1.14	8.13 ± 2.01	8.65 ± 2.04
30-39	7.39 ± 1.37	7.76 ± 1.13	8.12 ± 1.35	8.91 ± 2.25
40-49	8.32 ± 1.79	8.88 ± 1.65	9.39 ± 1.89	9.17 ± 1.45
50-59	9.19 ± 2.60	9.46 ± 2.45	9.93 ± 1.61	10.74 ± 1.78
60-69	9.12 ± 2.34	10.43 ± 2.65	10.86 ± 2.98	10.69 ± 2.42
≥70	9.80 ± 0.01	10.43 ± 0.92	10.55 ± 2.69	10.06 ± 1.82

BP: blood pressure; HT: arterial hypertension

Conclusions: In order to integrate arterial stiffness evaluation in clinical practice methodological standardization and reference values deduced form the general population evaluation are very much needed. Our data are answering to one of this goals for an emerging oscillometric method of PWV measurement.

PP.08.36 BLOOD PRESSURE AND ARTERIAL STIFFNESS IN RELATION TO SODIUM METABOLISM IN PATIENTS WITH DIASTOLIC LEFT VENTRICULAR DYSFUNCTION AND HIGH SODIUM INTAKE

M. Cwynar, J. Gasowski, B. Wizner, A. Gluszewska, J. Krolczyk, T. Grodzicki.
Department of Internal Medicine and Gerontology, Medical College, Jagiellonian University, Kraków, POLAND

Objective: Sodium load ranks among key mechanisms of the development of hypertension and its complications.

Design and method: In a population with high sodium consumption, we assessed relation between brachial and central blood pressures, elastic properties of large arteries, echocardiographic left ventricular diastolic function (LVDF) and sodium reabsorption in proximal (FELi) and distal (FDRNa) renal tubules assessed using the endogenous lithium clearance.

Results: We found a significant interaction between LVDF and FELi with respect to the values of brachial blood pressure: systolic (SBP), diastolic (DBP) and mean blood pressure (MBP) (all PINT<0.03). In patients with FELi, below the median value and impaired LVDF, the values of SBP (149.3 vs. 132.5 mmHg; P=0.005), DBP (85.1 vs. 76.1 mmHg; P=0.001), MBP (106.5 vs. 94.9 mmHg; P=0.001), central SBP (137.4 vs. 122.0 mmHg; P=0.01), central DBP (84.8 vs. 76.0 mmHg; P=0.003), central MBP (106.9 vs. 95.9 mmHg; P=0.007), central aortic pulse wave augmentation (AG) (18.0 vs. 13.5 mmHg; P=0.03), central aortic pulse wave augmentation index (AIxC) (155.7 vs. 140.9 %; P=0.01) and pulse wave velocity (PWV) (14.6 vs. 12.5 m/s; P=0.02) were significantly higher than in patients with normal LVDF. Such relationships were not observed in patients with FELi above the median value.

Conclusions: We conclude that in the hypertensive population with high sodium intake, increased sodium reabsorption in proximal tubules may affect blood pressures and arterial wall damage, thus contributing to the development of LVDF impairment.

PP.08.37 PATIENTS WITH TYPE 2 DIABETES MELLITUS HAVE GREATER PROPENSITY FOR A HYPERTENSIVE RESPONSE TO MODERATE INTENSITY EXERCISE: RELATION WITH LOCAL AND SYSTEMIC HAEMODYNAMICS

R. Climie, S. Nikolic, L. Keith, J. Sharman.
Menzies Research Institute Tasmania, Hobart, AUSTRALIA

Objective: A hypertensive response to moderate intensity exercise (HRE) is associated with increased cardiovascular mortality risk. Patients with type 2 diabetes mellitus (T2DM) have vascular irregularities which may predispose to an HRE at moderate intensity but this has not been examined previously. The aim of this study was to determine if patients with T2DM have propensity towards an HRE at moderate intensity exercise and also to examine the haemodynamic correlates of exercise blood pressure (BP).
Design and method: Sixty-eight patients with T2DM and 68 controls (56±9 vs 62±8 years, 57% male both) were examined at rest and during moderate cycle exercise (30 watts and 50 rpm). Haemodynamics recorded included; brachial and central BP and aortic stiffness (aPWV) by applanation tonometry; heart rate, stroke volume, cardiac output and systemic vascular resistance (SVR) by impedance cardiography. Moderate exercise HRE was defined as >160mmHg for females and >170mmHg for males.

Results: Patients with T2DM had significantly higher exercise brachial and central systolic BP (153±18 vs 137±16 mmHg, p<0.001 and 132±15 vs 117±12 mmHg, p<0.001), as well as a greater change from baseline (25±15 vs 17±23 mmHg, p=0.019). Nineteen patients with T2DM had an HRE compared to 4 controls (28% vs 6%; p=0.001). The strongest independent correlates of exercise brachial systolic BP in patients with T2DM were stroke volume and SVR (β=1.09, adjusted R^2=0.189, p=0.004 and β=-0.041, adjusted R^2=0.099, p=0.037 respectively) after adjusting for age, sex and body mass index. These variables were not associated with exercise brachial systolic BP in controls (β=0.421, adjusted R^2=0.052, p=0.120 and β=0.006, adjusted R^2=0.018, p=0.278 respectively).

Conclusions: Patients with T2DM have elevated BP responses to moderate intensity exercise and have greater prevalence of an HRE compared to controls. Abnormalities in central and peripheral haemodynamics may help explain exaggerated BP responses to exercise in patients with T2DM.

PP.08.38 EVALUATION OF CAROTID AND FEMORAL DIAMETER AFTER AN IRONMAN COMPETITION

E. Bianchini [1], R. Bruno [1,2], N. Di Lascio [1], A. Vezzoli [3], M. Mrakic Sposta [3], A. Corciu [1], M. Comassi [3], K. Ujka [1], R. Sicari [1], E. Picano [1], L. Pratali [1].
[1] Institute of Clinical Physiology, CNR, Pisa, ITALY, [2] Department of Internal Medicine, University of Pisa, Pisa, ITALY, [3] Institute of Bioimaging and Molecular Physiology, CNR, Milan, ITALY

Objective: The assessment of vascular functional properties in extreme exercise conditions could enhance the characterization of vessel properties, elucidating both dynamic behavior and modifications due to training. The aim of this study was to evaluate the acute effects of participation in Ironman triathlon competition on carotid and femoral properties, in relation to hemodynamic load.

Design and method: 28 male triathletes (41±8 years), participating at the Ironman competition (swimming 3.8 km, cycling 180 km, running 42,2 km; 13 athletes performed half-race), underwent cardiac, carotid and femoral ultrasound examinations at rest and within 20' from the arrival. For both arteries, mean arterial diameter (Dcar and Dfem) and distension were estimated by an automatic system applied to ultrasound B-mode image sequences, and pulse pressure (PPcar and PPfem) by tonometry; carotid and femoral cross-sectional compliance coefficients (CCcar and CCfem) were calculated.

Results: The mean duration of the competition was 12:48±1:14 h (6:14 ± 0:37 hrs for the half-race). At the end of the competition the athletes showed increased heart rate (from 60.2±13.1 to 82.8±15.6 bpm, p<0.0001), unchanged mean blood pressure (from 93±14 to 91±10 mmHg, p=ns), carotid PP (from 42 to 42 mmHg, p=ns), femoral PP (from 50±15 to 46±7 mmHg, p=ns), and stroke volume (from 64±14 to 59±16 ml, p=ns), in the presence of negligible dehydration (total body water from 48.0±4.0 to 46.5±3.9 kg, p=ns). Cardiac output increased (from 5.5±1.2 to 6.7±2.4 l/min, p<0.05), and total peripheral resistances were reduced (from 17.6±3.9 to 14.8±4.6, p=0.01). Dcar increased (from 7.19±0.65 to 7.61 ± 0.76 mm, p<0.05), while Dfem was unchanged at the end of the competition (10.41±0.83 and 10.49±0.82, mm p=ns). CCcar and CCfem were not modified (1.12±0.58 vs 1.22±0.54 and 0.99±0.40 vs 0.92±0.36 mm^2/KPa, p=ns).

Conclusions: In an Ironman competition, strenuous exercise induced a marked carotid dilation, but did not lead to vascular changes in the femoral artery, in the presence of unchanged blood pressure and hydration status. These data suggest a different acute functional adaptation in central arteries with respect to peripheral leg vessels.

PP.08.39 AORTIC TO BRACHIAL PULSE PRESSURE AMPLIFICATION AS FUNCTIONAL MARKER AND PREDICTOR OF RENAL FUNCTION LOSS IN CHRONIC KIDNEY DISEASE

M. Baumann [1], S. Wassertheurer [2], U. Heemann [1].
[1] Klinikum Rechts der Isar, Munich, GERMANY, [2] AIT, Vienna, AUSTRIA

Objective: Parameters associated with arterial stiffness and structural vascular remodeling, have been associated to renal function. Pulse pressure amplification (PPA) is a new parameter of arterial stiffness reflecting large artery function. Its contribution in chronic kidney disease (CKD) remains uncertain. We assessed the role of PPA in CKD and CKD progression in patients with CKD stage 2-4.

Design and method: CKD and CKD progression in patients with CKD stage 2-4. We studied a cohort of 128 (40% female) patients with CKD stages 2/3/4 (N=36/55/37), and 89 (49% female) controls. Each patient underwent a work-up including medical interview, clinical examination, blood sampling and determination of PPA.

Results: In cross-sectional analysis PPA was reduced in CKD patients as compared to control subjects. In CKD patients reduced PPA was associated with a decline in renal function. Prospective follow-up was 42 months. Sixteen renal endpoints defined by 50% loss of renal function or start of renal replacement therapy were detected during this period. In Cox regression analysis PPA, eGFR and proteinuria predicted renal endpoints. There was an interaction between CKD and PPA present. Stratification according to CKD severity and median of PPA revealed that CKD stage 4 and low PPA had the highest risk to develop renal endpoints unadjusted 8.1 (2.4 – 27.7) and adjusted for age and proteinuria 5.6 (1.5 – 21.9). This was confirmed by Kaplan-Meier analysis (log-rank P<0.001).

Conclusions: Taken together, PPA is reduced in CKD, associated with declining renal function and low PPA predicts renal endpoints in severe CKD.

PP.08.40 AORTIC ANEURYSM AND DISSECTION IN HYPERTENSIVE PATIENTS: A RARE COMPLICATION BUT BEING ABLE TO BURN IN NORTH AFRICA

N. Ali-Tatar Chentir, S. Alane, M.T. Chentir.
Mustapha University Hospital, Algiers, ALGERIA

Objective: An aortic aneurysm is a localized dilatation of the aorta greater than 50% the normal diameter and it should include the three layers of the wall. One of the main causes includes hypertension. Echocardiography is a very useful diagnostic tool for aortic aneurysm assessment. Transthoracic echocardiography TTE is the first- choice diagnostic tool for this indication and trans-oesophageal echocardiography (TOE) is used if additional information is required. The aim or our study is to analyze the profile of our hypertensive patients (pts)who develop an aortic aneurysm.

Design and method: We performed a prospective study starting from October 2010 to 2013, on 60 consecutive hypertensive patients mean age 63±14 years, 52 male 8 female . They underwent clinical, ECG, TTE and TOE examination for assessment of aortic aneurysm. If dissection is present, the De Bakey classification is used: type I if it involves the entire aorta; type II dissection if it involves the ascending aorta and type III if it involves the descending aorta.

Results: 24 pts (40%) have association of hypertension, diabetes mellitus tobacco smoking; 30pts have the combination of hypertension-dyslipidaemia and tobacco smoking. 6pts(10%) presents an abdominal aneurysm; 24pts (40%) aneurysm of the ascending aorta; type III dissection in 16pts(26%); dissection type II in 7pts (11%)who underwent Bentall procedure and in 8 (13%)pts the entire aorta is involved , type I dissection from the De Bakey classification. All the patients didn't reach the Blood pressure goal.

Conclusions: Patient participation and reduction of physician inertia are fundamental components against uncontrolled hypertension, diabetes, tobacco smoking and obesity.

PP.08.41 CAROTID ARTERY ECHOGENICITY AND CENTRAL ARTERY HAEMODYNAMICS IN HEALTHY MIDDLE-AGED AND OLDER INDIVIDUALS

K. Aizawa [1,2], F. Casanova [1,2], D. Mawson [1,2], K.M. Gooding [1,2], S. Elyas [1,2], D.D. Adingupu [1,2], W.D. Strain [1,2], A.C. Shore [1,2], P.E. Gates [1,2].
[1] University of Exeter Medical School, Diabetes and Vascular Medicine Research Centre, Exeter, UNITED KINGDOM, [2] NIHR Exeter Clinical Research Facility, Exeter, UNITED KINGDOM

Objective: Grey scale median of the common carotid artery intima-media complex (IM-GSM) is a recently introduced ultrasound-based assessment to characterize the composition of arterial wall. Echogenic carotid artery plaque has been shown to be associated with increased aortic stiffness. It is unknown if a similar association exists between IM-GSM and aortic stiffness as well as between IM-GSM and other central artery haemodynamic indices. This study examined the relationship between IM-GSM, aortic stiffness and central artery haemodynamics in healthy middle-aged and older individuals.

Design and method: Data from 86 individuals (63.5±8.6yrs, 43F) who had no overt cardiovascular disease and were not on any medications were analyzed in this study. Common carotid artery diameter, far-wall intima-media thickness (IMT) and blood velocity data were obtained using ultrasound. IMT and IM-GSM were analyzed using semi-automated edge-detection software. Aortic stiffness assessed by carotid-femoral PWV (cfPWV) and aortic blood pressure estimated from radial artery tonometry and generalized transfer function were obtained using a commercially available apparatus (SphygmoCor®). Carotid artery wall shear rate (WSR) was estimated using peak, mean and diastolic blood velocity data.

Results: IM-GSM was inversely associated with IMT (r=-0.50), aortic SBP (r=-0.39), aortic pulse pressure (PP; r=-0.40), MAP (r=-0.26) and cfPWV (r=-0.43, all p<0.05). IM-GSM was also inversely associated with body mass index (r=-0.25) and blood glucose concentration (r=-0.25, both p<0.05). None of the estimated WSR indices were associated with IM-GSM. In a stepwise multivariate regression analysis, IMT, body mass index and aortic PP were each independent determinants of IM-GSM (total R^2=0.40). This association was unaffected by the addition of brachial PP into the model.

Conclusions: These results suggest an unfavourable influence of increased IMT, aortic PP and body mass index on carotid artery wall composition.

PP.08.42 CAROTID ARTERY ECHOGENICITY AND CENTRAL ARTERY STIFFNESS IN TYPE 2 DIABETES: CO-EXISTENCE OF HYPERTENSION AND CARDIOVASCULAR DISEASE

K. Aizawa [1,2], F. Casanova [1,2], D. Mawson [1,2], K.M. Gooding [1,2], S. Elyas [1,2], D.D. Adingupu [1,2], W.D. Strain [1,2], A.C. Shore [1,2], P.E. Gates [1,2].
[1] University of Exeter Medical School, Diabetes and Vascular Medicine Research Centre, Exeter, UNITED KINGDOM, [2] NIHR Exeter Clinical Research Facility, Exeter, UNITED KINGDOM

Objective: Type 2 diabetes (DM) is known to increase aortic stiffness, an independent predictor of future cardiovascular disease (CVD). Co-existence of DM and hypertension (HT) has also been shown to further increase stiffness. Grey scale median of the common carotid artery intima-media complex (IM-GSM) is thought to reflect the composition of arterial wall (atherosclerotic changes). However, it is unclear whether the co-existence of DM with HT or with HT and CVD alters IM-GSM, similarly to aortic stiffness. This study examined IM-GSM and aortic stiffness in middle-aged and older DM individuals with and without the co-existence of HT and with HT and CVD.

Design and method: Data from 325 individuals were included and divided into 4 groups: 86 healthy control (CT; 63.5±8.6yrs, 43F), 64 DM only (DO; 63.8±8.5yrs, 23F), 85 DM and HT (DH; 66.4±8.4yrs, 32F), and 90 DM, HT and CVD (DHC; 67.9±8.7yrs, 17F). Common carotid artery far-wall intima-media thickness (IMT) image was obtained using ultrasound. IMT and IM-GSM were analyzed using semi-automated edge-detection software. Aortic stiffness was assessed by carotid-femoral PWV (cfPWV) using applanation tonometry.

Results: DHC group was older than CT and DO groups (p<0.05). IM-GSM was unfavourably altered in DO (104.7±2.9au), DH (105.1±2.5au) and DHC (101.7±2.5au) compared to CT (122.5±2.5au, p<0.05) after adjustment for age and sex. Adjustment for IMT did not change this finding. Accumulation of risk factors stiffened the aorta, indicated by increased cfPWV (CT, 9.1±0.2m/s; DO, 10.2±0.3m/s; DH, 10.4±0.3m/s; DHC, 10.7±0.3m/s; p<0.05) after adjustment for age and sex. Multivariate regression analysis showed that the presence of DM was independently associated with IM-GSM in addition to IMT and body mass index in the full pooled data set (total R^2=0.28).

Conclusions: These results demonstrate that the presence of DM itself unfavourably alters IM-GSM without further influence from the co-existence of HT or CVD, while aortic stiffness does not show such a clear-cut difference in our population. These findings suggest that alterations in IM-GSM may be an early marker of atherosclerotic vascular changes associated with DM.

PP.08.43 IMPLICATIONS OF REACTIVE OXYGEN SPECIES (ROS) FOR AORTIC CALCIFICATION IN CHRONIC KIDNEY DISEASE

R. St-Louis, A. Gauthier-Bastien, F. Mac-Way, R. Ung, S. Mokas, R. Larviere, D. Richard, M. Agharazii. *Centre de recherche du CHU de Quebec, Hotel-Dieu de Quebec, Faculty of Medicine, Université Laval, Quebec City, CANADA*

Objective: Vascular calcification is a consequence of finely regulated processes in patients suffering from chronic kidney disease (CKD). Many factors are able to induce the transdifferentiation of vascular smooth muscle cells (VSMC) towards an osteoblast-like phenotype, including oxidative stress and reactive oxygen species (ROS). There are important links between cytokine activation, ROS generation and CKD. While inflammation may play a role in atherosclerotic (intimal) vascular calcification, inflammation and ROS are generally not considered to play a dominant role in medial vascular calcification. Here, we used an animal model of medial vascular calcification in CKD to assess the importance of inflammatory cytokines, ROS generators and downstream signaling events during vascular calcification.

Design and method: Wistar rats were rendered uremic by a 5/6 nephrectomy procedure. Vascular calcification was induced by a high calcium (Ca) and phosphorus (P) diet supplemented with vitamin D3 diet (CKD+Ca/P/VitD). Between experimental weeks 3 and 6, hemodynamic parameters and pulse wave velocity were assessed. At the end of experimental week 6, blood and thoracic aortas were collected for analysis, which included tissue immunofluorescence studies along with RNA and protein expression assays.

Results: CKD+Ca/P/VitD rats showed increased pulse pressure, pulse wave velocity and marked calcification of the aortic media. Animals with vascular calcification demonstrated the presence of macrophages near the sites of calcification.The expression of the inflammatory cytokines TNF, IL-1β and IL-6 were all increased in aortas from treated animals. Additionally, while the expression of main antioxidant enzymes were diminished in aortas from treated animals, the expression of essential subunits of an important ROS generator, NADPH oxidase, were increased. Finally, specific signaling pathways, known to be targets of increased ROS, were activated in aortas from treated animals.

Conclusions: Our study indicates that in an animal model of chronic kidney disease, proinflammatory cytokines and ROS generation participate in signaling pathways involved in vascular calcification. This work shows that a close relationship exists between oxidative stress, inflammatory responses and arterial medial calcification during CKD.

POSTERS' SESSION

POSTERS' SESSION PS09
MOLECULAR BIOLOGY - NEURAL AND MEMBRANE MECHANISMS

PP.09.01 ROLE OF MEMBRANE POTASSIUM CONDUCTANCE IN THE MECHANISMS OF HYDROGEN SULFIDE VASORELAXING ACTION

L. Smagliy [1], A. Marchenko [1], U. Birulina [1], S. Gusakova [1], I. Kovalev [1], S. Orlov [2].
[1] Siberian State Medical University, Tomsk, RUSSIA, [2] Laboratory of the Research Center of the University of Montreal, Montreal, CANADA

Objective: Hydrogen sulfide (H2S) plays an important role in the regulation of the blood vessels smooth muscles tone. It leads to a strong relaxation of the vascular wall principally due to the activation of smooth muscle cells (SMC) membrane potassium channels.

Design and method: The study was performed by the method of mehanography on endothelium-denuded aortic smooth muscle segments of the Wistar rats. SMC contractions were induced with highpotassium solution (30mM KCl) and α1-adrenomimetic phenylephrine (PE, 10μM). The amplitude of contractions was calculated as a percentage of the control contraction induced with 30KCl or PE. We used sodium hydrogen sulfide (NaHS) as a donor of H2S. Potassium channels activity was modulated by relevant potassium channels blockers.

Results: In SMC precontracted with 30KCl addition of 5-50μM NaHS increased mechanical tension of SMC, and addition of 100-1000μM NaHS decreased it in dose-dependent manner. We tested the effect of 500μM NaHS (EC50), relaxing action of which was 35.1±7.5% (n=6, p<0.05) of the amplitude of the control highpotassium contraction. Blocker of calcium-activated and voltage-dependent potassium channels tetraethylammonium (TEA, 10mM) significantly reduced NaHS relaxing effect, which was 13.9±3.2% (n=6; p<0.05). Voltage-dependent potassium channels blocker 4-aminopyridine (4AP, 1mM) had no effect on NaHS-induced relaxation. Blockers of large conductance calcium-activated potassium channels and ATP-sensitive potassium channels charybdotoxyn (HT, 0.1μM) and glibenclamide (GB, 10μM), respectively, both increased relaxing effect of NaHS.
In SMC precontracted with PE addition of 5-1000μM NaHS decreased mechanical tension of SMC with EC50=100μM and the value of relaxation 55.8±7.2% (n=6, p<0.05) of the control PE-induced contraction. TEA (10mM) and 4AP (1mM) both significantly reduced relaxing effect of 100μM NaHS to 13.8±5.2% (n=9, p<0.05) and 16.2±2.7% (n=7, p<0.05) respectively. GB (10μM) completely abolished the relaxing effect of 100μM NaHS. HT (0.1mM) had no significant effect on H2S- induced relaxation.

Conclusions: In contraction induced by depolarization of SMC membrane with highpotassium solution, relaxing effect of H2S is mediated by opening of calcium-activated potassium channels of small and intermediate conductance, and in SMC contraction induced by activation of α1-adrenergic receptors – by activation of ATP-sensitive potassium channels.

PP.09.02 INFLUENCE HYDROGEN PEROXIDE ON PULMONARY ARTERY OF GUINEA PIGS

A. Nosarev, T. Kironenko, A. Kedenova.
Siberian State Medical University, Tomsk, RUSSIA

Objective: Hydrogen peroxide - the representative of reactive oxygen species, can perform in the body's cells as a function of the signal, and is a metabolite of damaging surrounding tissue. The concentration of hydrogen peroxide may vary considerably, affecting the mechanical stress in vascular smooth muscle. Of particular importance, this fact may have in various diseases, such as hypertension, diabetes mellitus. Hence the need for the present study.

Design and method: The study was performed by mechanographics metod smooth muscle isolated ring segments of pulmonary artery of guinea pigs . Precontracture was caused by high potassium Krebs solution (40 mM KCl).

Results: Hydrogen peroxide at concentrations ranging from 0.001 pM to 1000 pM constrictor has a direct dose-dependent effect on precontracted pulmonary artery smooth muscle. Growth strain amounted to 45 % of the high potassium contraction of the segments remote from the endothelium, and 59 % - stored for segments with endothelium.

Conclusions: Hydrogen peroxide has a constrictor action on precontracted smooth muscle of guinea pig pulmonary vessels, which may have pathogenetic importance in diseases such as pulmonary hypertension and other.

PP.09.03 GENETIC PREDISPOSITION TO CARDIOVASCULAR DISEASES IN THE OFFSPRING OF POPULATION EXPOSED TO RADIATION IN RESULT OF NUCLEAR TESTS

A. Markabayeva [1], L. Pivina [1], A. Kerimkulova [1], T. Belikhina [2], A. Adylkhanova [2], A. Akhmetova [1]. *[1] Semey State Medical University, Semey, KAZAKHSTAN, [2] Research Institute for Radiation Medicine and Ecology, Semey, KAZAKHSTAN*

Objective: This study of genetic predisposition to developing of cardiovascular diseases (CVD) in the offspring of population exposed to radiation.

Design and method: Analysis of frequency of Met235Thr and Thr174Met polymorphisms gene AGT, Leu 28 Pro gene APOE, C786T gene NOS3, Glin192Arg gene PON1 and Lys198Asn gene EDN1. Total 218 people were examined. Selection was based on the family principle including 27 persons of age group 60 > (I generation of persons exposed to direct radiation), 141 their children (II generation) and 50 grandchildren (III generation).

Results: It was found high frequency of heterozygous type inheritance for Thr174Met polymorphisms gene AGT (46.15 %; 48.9 %, and 52.0 % respectively in I, II, and III generations); for people of I, and III generations heterozygous type prevailed over homozygous. For Met235Thr frequency of heterozygous type in the offspring of exposed people was higher compared with I generation (48.15; 51.2 %, and 54.0 % respectively in I, II, and III generations (p<0.05; 0.05)).
Heterozygous type inheritance for APOE Leu28Pro was dominant in the II and III generations (51.64 % and 50.0 % respectively; 19.23 % in I generation (p<0.05; 0.05). Homozygous mutant type inheritance in the offspring of III generation (age <30) was 8.33 % versus 1.64 % in II generation (p<0.01; 0.01).
It was found unexpected high frequency of monozygotic pathological mutations for NOS3 C786T genotype in the people of I and III generation (26.1 % and 20.83 % respectively). Frequency of heterozygous type inheritance for genotype EDN1 Lys198Asn was 36.0 %, 38.62 %, and 39.58 % respectively.

Conclusions: Results of study indicate the possible inheritance of pathological mutations of genes responsible for developing of disorders of lipid metabolism, endothelial dysfunction and hypertension in the offspring of exposed to radiation people.

PP.09.04 THE ROLE OF NITRIC OXIDE IN THE MECHANISM OF ACTION OF CARBON MONOXIDE ON THE CONTRACTILE ACTIVITY OF SMOOTH MUSCLE CELLS FROM THE RAT AORTA

A. Marchenko, J. Birulina, S. Gusakova, I. Kovalev, L. Smagliy.
Siberian State Medical University, Tomsk, RUSSIA

Objective: To study the mechanism of carbon monoxide action on the contractile responses of vascular smooth muscle cells.

Design and method: Contractile responses of rat aorta strips triggered by depolarization and activation of α1-adrenergic receptors with high K+-medium and phenylephrine, respectively, were measured as increments of isometric tension. Tricarbonyldichlororuthenium(II)-dimer (CORM-2) was used as a donor of carbon monoxide. ODQ (1μM), L-NAME hydrochloride (100 μM) of used to inhibit NO-synthase and soluble guanylate cyclase. To elucidate the contribution of changes in membrane conductance potassium blockers used: Tetraethylammonium chloride (10mM) and 4-Aminopyridine (1mM).

Results: It is shown that the donor of carbon monoxide - CORM-2, in experiments with of high potassium contraction in concentrations of 10-1000 μM, and in cases phenilefrine-induced contractions (10 μM) of smooth muscle cells, of 1 μM and above, caused a dose-dependent relaxation of vascular segments. Inhibition of NO-synthase and soluble guanylate cyclase (GC) weakened CO - induced relaxation of the segments. With blocking potassium channels tetraethylammonium chloride and 4-aminopyridine relaxing effect CORM-2 on vascular segments virtually eliminated.

Conclusions: These results may be the evidence of cooperation in the implementation of gazotransmitters gasotransmitters relaxating effect of carbon monoxide on the level of soluble guanylate cyclase and potassium channels plasmalemma of smooth muscle cells.

PP.09.05 PERSISTENT SIGNIFICANT ELEVATION OF CK WITH UNKNOWN ETIOLOGY

A. Hallak [1], O. Hallak [1], A. Alshammaa [1], L. Aljundi [1], O. Shehab [2], A. Zarzour [3], Q. Radaideh [4], O. Tujjar [5], O. Hallak [6]. *[1] University of Sharjah, Sharjah, UNITED ARAB EMIRATES, [2] UAE University, Abu Dhabi, UNITED ARAB EMIRATES, [3] Jordan University of Science and Technology, Irbid, JORDAN, [4] University of Jordan, Amman, JORDAN, [5] Università degli Studi di Palermo, Florence, ITALY, [6] American Hospital Dubai, Dubai, UNITED ARAB EMIRATES*

Objective: Case report about idiopathic hyperCKemia.

Design and method: 52yo male with history of dyslipidemia, smoking, and alcohol abuse, with no hypertension, no DM, presented on 9/1/09 with acute MI with occluded RCA. He underwent a drug-eluting stent to RCA with excellent angiographic result. The hospital course was unremarkable. At presentation, total CK (Creatine Kinase) was 352 U/L which peaked at 700, CKMB 4.2 U/L and TROP T < 0.01 U/L. Patient discharged on aspirin, clopidogril, metoprolol, and atorvastatin 80mg. 16/10/09, presented with mild muscle aches after exercising for 2 hours. CK > 20,000, CKMB 49.23, TROP T 0.02. His liver test, renal function and CBC are normal, and myoglobin 2.15. Patient was treated with IV fluid, continued on aspirin and clopidogril; statin was held. Repeat CK gradually dropped to 2,230. Patient was asymptomatic throughout the hospital course, and on 29-12-2009 the ck 1529, normal renal, pt still off statin. Repeat investigations over the period of 2 years continued to show persistent elevation in CK in the 1300 range. In Feb 2012 add rovastatin. August ldl 1.9 ck 1052.

Results: Muscle biopsy shows slight variation in fiber diameter, non-specific, slight increase lipid storage in some fibers not sufficient to diagnose of lipid storage myopathy. Aldolase serum 9.5, ANA negative Electrophoresis of ck; 99.1 mmck, 0.9 mbck, 0.0 bbck, thyroid function normal.

Conclusions: This middle-aged male presented with acute MI. Lab investigations showed elevated CK in the 300 range. Later it dropped as expected then back up to 20,000 after vigorous exercise and continued to be elevated in the 1,200 range for several years.
The work up was unrevealing, the possible contributing factors such as statin and alcohol were removed. Autoimmune diseases also ruled out. This elevation of CK was triggered by muscle trauma (vigorous exercise) but persisted for a long time without any further injury. Patient has no muscle pain or weakness. There is probably a lack of filtering out the CK from the body rather than increased production from muscle destruction. In this case we couldn't find a definite explanation and call it idiopathic hyperCKemia.

PP.09.06 EPIGENETIC REGULATION OF HUMAN KIBRA EXPRESSION

K. Guske [1], B. Schmitz [1,2], G. Ciarimboli [1], S. M. Brand [2], E. Brand [1].
[1] University Hospital Münster, Internal Medicine D, Nephrology, Hypertension and Rheumatology, Münster, GERMANY, [2] University Hospital Münster, Institute of Sports Medicine, Department of Molecular Genetics of Cardiovascular Disease, Münster, GERMANY

Objective: KIBRA has been described as a key factor of the Hippo signaling pathway, which controls organ size and cell growth, cell contact inhibition as well as tumorigenesis and cystogenesis. Dysregulation of Hippo pathway components including KIBRA have been described in human cancer development. In the current work, we analyzed the epigenetic regulation of human KIBRA expression based on a detailed analysis of the KIBRA 5'-regulatory region. We determined specific KIBRA methylation patterns in different renal cell carcinoma subtypes and the impact of methylation on KIBRA expression.

Design and method: We analysed the functional impact of KIBRA CpG islands methylation in reporter gene assays using the CpG-free pCpGL-basic vector system. Promoter deletion constructs were methylated in vitro using methyltransferases SssI or HpaI and transfected into human neuroblastoma (SH-SY5Y) and kidney epithelial (IHKE) cells. Genomic DNA was isolated from kidney tissues of patients with different carcinoma subtypes (e.g. clear cell, papillary, chromophobe), bisulfite converted, subcloned and sequenced. De novo KIBRA demethylation was analyzed in all cell lines treated with 5-azacytedine and trichostatine A.

Results: We identified two separate methylation-sensitive CpG islands located within the KIBRA core promoter (CpG1) and an alternative promoter (CpG2). Methylation of all CpG sites by SssI resulted in a total abrogation of the promoter activity in vitro, while partial methylation by HpaII only repressed the CpG1 promoter activity in IHKE cells. Bisulfite sequencing of subcloned patients' DNA revealed significant differences in methylation patterns of CpG1 and CpG2. Promoter demethylation in vivo by 5-azacytedine and trichostatine resulted in an activation of KIBRA expression in SH-SY5Y cells.

Conclusions: KIBRA expression depends on specific methylation patterns of at least two functional CpG islands. The impact of partial promoter methylation on KIBRA expression was cell-type specific, which underlines our previous results demonstrating differential KIBRA regulation in renal and neuronal cells. Based on our data, we suggest an association of KIBRA methylation status with different renal carcinoma subtypes.

PP.09.07 EFFECT OF HIGH GLUCOSE AND ANGIOTENSIN II IN ATRIAL FIBROBLASTS OF FAILING HUMAN HEARTS

T. Fiaschi [1], F. Magherini [1], T. Gamberi [1], A. Modesti [1], P. Modesti [2]. *[1] Department of Biomedical, Experimental and Clinical Sciences Mario Serio, University of Florence, Florence, Italy, Florence, ITALY, [2] Critical Care Medicine and Surgery, University of Florence, School of Medicine, Florence, ITALY*

Objective: Cardiac fibroblasts significantly contribute in inducing structural and functional changes in the heart. Despite several evidences about ventricular fibroblasts, a small number of studies have been made on atrial fibroblasts. In atrial myocardium, activation of local renin-angiotensin system and mitogen-activated protein kinase pathways plays essential role in atrial structure remodeling. In particular, the effect of angiotensin (ang) II is due to the activation of Janus kinase signal transducers and activators of transcription (JAK-STAT) pathway. The objective of the present study was to describe the effects of Ang II stimulation on JAK2/STAT3 Tyr-phosphorylation in human failing atrial fibroblasts.

Design and method: Fibroblasts were isolated from right atrial appendages of failing human hearts (n=3) and passaged three times to yield almost pure cultures (>99% purity). Cells were changed to serum free medium for 24 h, exposed to media containing glucose 5nM (NG) or 25 mM (HG) for 2h, and stimulated with ang II (100 nM) for 5, 10, 15, 30 and 60 minutes, respectively. JAK2 (Tyr-1009) and STAT3 (Tyr-705) phosphorylation were then investigated by Western blot analysis using specific antibodies.

Results: Our results show that Ang II stimulation fails to induce phosphorylation both of JAK2 and STAT3 proteins in NG condition. Furthermore, HG condition, that we previously observed to induce both JAK2 and STAT3 tyrosine phosphorylation in ventricular fibroblasts, is not able to activate JAK2 and STAT3.
Conclusions: Present findings indicate that neither ang II stimulation and HG can induce JAK2 and STAT3 tyrosine phosphorylation in human failing atrial fibroblasts (at least at the considered times). Our previous results showed that ang II and HG alone induced both JAK2 and STAT3 tyrosine phosphorylation leading to increased collagen I deposition in ventricular fibroblasts. Ongoing studies are aimed to investigate the causes of the different effects of HG and ang II stimulation in atrial and ventricular fibroblasts.

PP.09.08 MISO THE TRADITIONAL JAPANESE FERMENTED FOOD, AND EFFECT ON THE BAROREFLEX SENSITIVITY OF THE HEART AND ARTERY

T. Yambe, H. Miura, Y. Shiraishi. *Tohoku University, Sendai, JAPAN*

Objective: Several kinds of the Japanese conventional style foods have been thought to be one of the most important food habit in the candidates to prevent the hypertension. In order to determine the effect of the Miso, which was the conventional and historical Japanese style natural fermented food, the newly developed quantitative baroreflex evaluating device (Jpn Pt.4789203) has been used in this study.

Design and method: 12 healthy adult volunteers had been used in the experiments after the ethical commitee allowance. Coffee and alcohol intake was prohibited before the experiments. Type A behavior pattern, hostility score, and beck depression scale were calculated from the Questionnaire before the measurements. Finger chip pulse wave, blood pressure and ECG were recorded in the data recorder at the sitting position and various kinds of audiovisual contents were added to the subjects. Quantitative analysis, Power spectral analysis of the time series data was carried out, and cross correlation function, transfer function and gain were calculated from the each power spectral data. HRV and fluctuations were calculated from power spectrum, and baroreflex function was calculated from the slope of the regression line between the blood pressure change and HR. And baroreflex function of the artery was calculated from the regression line between pulse tranmission time (PTT) and blood pressure changes with time lag calculated from the cross correlation function.

Results: As the results, significant correlation was observed between the some Questionnaire data and Miso intake habit and hemodynamic spectral data. For example, type A behavior pattern scale and the hostility scores of the subjects had the significant correlation with the miso intake habits. Rho max suggesting the linearity of the spectral data showed the significant difference in pulse wave transmission time and blood pressures.

Conclusions: Our results had suggested that eating habit had the effect on the autonomic nervous system baroreflex sensitivity. Traditional japanese foods might have the merit in hypertension control. Further consideration will be needed for the eating habits and Miso intake, because it have the economical advantage compared with the drug administration.

PP.09.09 CAPSAICIN MEDIATED AFFERENT RENAL DENERVATION: PHARMACOLOGICAL CONFIRMATION AND IMPLICATIONS FOR THE PATHOPHYSIOLOGY OF HYPERTENSION

R. Wainford. *Boston University, Department of Pharmacology, Boston, MA, USA*

Objective: It has been reported that capsaicin evokes selective denervation of the renal afferent nerves. We assessed the efficacy of capsaicin-mediated denervation in preventing the physiological responses to activation of the renal afferent and efferent nerves and in the development of dietary salt-evoked hypertension in the Dahl salt-sensitive rat.

Design and method: Conscious Sprague-Dawley (SD) rats implanted with an ICV cannula, having undergone sham (S) or bilateral renal afferent nerve denervation (ADNX) (capsaicin 33mM), received IV and IR infusions of bradykinin (BK) (5-40 µg/kg/min) and adenosine (A) (2-12 µg/min). All animals then received ICV guanabenz (50µg) (N=5/gp). HR, MAP and urinary sodium excretion (UNaV) were continuously monitored. Dahl salt-sensitive (DSS) rats underwent sham, ADNX or bilateral RNDX surgery (N=5/group) – all animals were maintained on an 8% NaCl diet for 21-days and MAP was continuously monitored by radiotelemetry.

Results: IR, but not IV, BK dose-dependently increased MAP and HR in sham, but not ADNX rats (BK 40 µg/kg/min; peak change HR [bpm] S +61±8 vs ADNX -5±3, P<0.05; peak change MAP [mmHg] S +19±3 vs ADNX +0.6±2, P<0.0.5). IR, but not IV, adenosine evoked a dose-dependent increase in natriuresis in sham animals, a response abolished by ADNX (A 12 µg/min; peak change UNaV [µeq/min] S +18.7±3 vs ADNX +2±0.4, P<0.05). In both sham and ADNX rats, ICV guanabenz evoked profound natriuresis (guanabenz 50 µg; peak change UNaV [µeq/min] S +13.4±1 vs ADNX +12.8±1). In DSS rats a high salt diet evoked hypertension in sham rats, hypertension was attenuated in RDNX rats but exacerbated in ADNX rats (DSS High-salt diet day 21 peak change MAP [mmHg]; S +30±3, RDNX +20±2*, ADNX +45±6*, P<0.05).

Conclusions: Capsaicin mediated afferent renal denervation prevents the physiological responses to intrarenal administration of activators of the renal afferent nerves without affecting the function of the renal efferent nerves - indicated by the natriuresis to central α2-adrenoceptor stimulation. Afferent renal denervation exacerbated DSS hypertension – suggesting a critical role of the renal afferent nerves as a CNS negative feedback mechanism to evoke efferent renal nerve (and global) sympathoinhibition and the attenuation of hypertension.

PP.09.10 CARDIOVASCULAR REACTIVITY DURING DRIVE TEST SIMULATION: COMPARISON BETWEEN HYPERTENSIVE PATIENTS ON THERAPY WITH ATENOLOL AND NORMOTENSIVE SUBJECTS

L. Grosso Di Palma [1], E. Gallazzi [2], V. Gagliardi [2], R. Meazza [2], G.L. Perrucci [4], A. Villarini [2,3]. *[1] William Harvey Research Institute within Barts and the London School of Medicine and Dentistry, Queen Mary University, London, UNITED KINGDOM, [2] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, ITALY, [3] Dipartimento di Medicina Predittiva e per la Prevenzione, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, ITALY, [4] Centro Cardiologico Monzino-IRCCS, Laboratorio di Biologia Vascolare e Medicina Rigenerativa, Milan, ITALY*

Objective: In previous studies, we were able to demonstrate the ability of the drive test simulation to stimulate a cardiovascular response in normotensive patients with a mixed pattern characterized by a dominant vascular component. This reactivity was particularly evident in the female population and there was a gender-dependant difference during high speed street driving and manoeuvres, characterized by females cardiovascular reactivity to be more stimulated by manoeuvres and males by high speed. The aim of this study was to evaluate the influence of a drive test simulation on the cardiovascular reactivity of hypertensive patients on b-blockers therapy and to compare it with normotensive patients.

Design and method: 67 patients (52 normotensive and 15 hypertensive on atenolol 100 mg/day therapy, 31 males and 36 females, mean age 40±8 years old) underwent a drive test with a car simulator. We continuously monitored in a non invasive way systolic and diastolic blood pressure, heart rate, stroke volume, cardiac output and total peripheral resistances. Following operator directions, patients underwent a standardized route consisting of high speed street driving and manoeuvres in narrow and crowded places.

Results: The reactivity of the hypertensive population on atenolol and the normotensive one resulted statistically different during drive test, as shown in Table. No statistically significant differences in reactivity between gender in the hypertensive population was found (all p=ns).

	Δ (speed – baseline) Atenolol	Δ (speed – baseline) Controls	P
SYS [mmHg]	9,23 (± 2,59)	24,2 (± 18,05)	0,002
DIA [mmHg]	8,51 (± 5,12)	21,0 (± 13,21)	0,001
HR [bpm]	6,6 (± 2,48)	8,2 (± 9,37)	0,510
SV [ml]	0,39 (± 5,3)	-7,68 (± 15,7)	0,055
CO [lpm]	0,56 (± 0,38)	-0,15 (± 1,21)	0,027
TPR [mmHg/mlps]	-0,3 (± 0,1)	0,27 (± 0,33)	0,001
	Δ (manoeuvres – baseline) Atenolol	Δ (manoeuvres – baseline) Controls	P
SYS [mmHg]	15,89 (± 2,12)	30,36 (± 17,39)	0,002
DIA [mmHg]	15,07 (± 1,83)	25,31 (± 13,28)	0,004
HR [bpm]	9,02 (± 1,84)	9,81 (± 11,4)	0,790
SV [ml]	0,29 (± 7,17)	-8 (± 16,46)	0,060
CO [lpm]	0,76 (± 0,5)	-0,16 (± 1,38)	0,013
TPR [mmHg/mlps]	0,02 (± 0,16)	0,36 (± 0,4)	0,002

Conclusions: When comparing normotensive and hypertensive on atenolol, the results have shown the effect of b-blockers on reducing cardiovascular reactivity during a stressor test. The fact that there were no differences between genders in the hypertensive population emphasizes the role of atenolol in reducing gender-dependant differences in the cardiovascular reactivity that was demonstrated in the normotensive population.

PP.09.11 HYPNOTIC FOCUSED ANALGESIA AND HYPNOTIC GENERAL ANAESTHESIA PREVENT THE CARDIOVASCULAR EFFECTS OF PAIN. PILOT STUDY

P. Rempelou [1], N. Giordano [1], C. Paladini [1], M. Giacomello [2], A.M. Lapenta [1], M.T. Tosello [1], A.M. Rossi [1], G. Regaldo [1], F. Russano [1], V. Tikhonoff [3], E. Facco [4], E. Casiglia [3]. *[1] Italian Centre for Clinical and Experimental Hypnosis, Turin, ITALY, [2] Institute of Anaesthesia, Hospital of Padua, Padua, ITALY, [3] Department of Medicine, University of Padua, Padua, ITALY, [4] Department of Neurosciences, University of Padua, Padua, ITALY*

Objective: To establish whether Hypnotic focused analgesia (HFA) corresponding to local anaesthesia and hypnotic general anaesthesia (HGA) corresponding to spontaneous-breathing general anaesthesia are able to prevent the central and peripheral resistance rise induced by painful stimuli on the median nerve (PSMN).

Design and method: Hypnotic induction was obtained in 5 normal volunteers. Hand HFA was suggested as described in Casiglia et al, Hypnosis prevents the cardiovascular response to cold pressor test, Am J Clin Hypn 2007:49:255-66. HGA was obtained in the same subjects suggesting total-body analgesia, narcosis, muscular immobility and amnesia like. PSMN was produced through a device giving direct current (DC) electric discharges (2 stimuli/second). HGA differed from HFA in that, analgesia was extended to total body, hypnotic sleep reproducing surgical narcosis was induced, paralysis was suggested but for respiratory muscles and subjects did not know where the painful stimuli would be administered. Subjective pain (SP) was recorded with a 0-10 visual scale. Maximum tolerable DC intensity indicated objective pain tolerance (OPT). Blood pressure, forearm flow and cardiac output were monitored, and central and peripheral resistance were calculated in normal consciousness, in HFA and in HGA in order to measure the adrenergic response triggered by pain stimuli (ARPS).

Results: SP: in comparison to pre-hypnotic conditions, maximum subjective pain decreased in average by 84% in HFA and 111% in HGA. OPT: at the maximum PSMN, pain tolerance increased by 30% in HFA and by 64% in HGA. Haemodynamics: in basal conditions, the PSMN inducing maximum tolerable pain produced 46% increase of central resistance and 46% increase of peripheral resistance, while during HFA and during HGA no increase of resistance was observed.

Conclusions: HFA significantly reduces subjective pain perception, an effect that is mirrored by objective pain tolerance. HGA is even more efficient than HFA in this respect. What is more important, both HFA and HGA significantly reduce the ARPS, so living organ protection against pain. Consequently, both HFA and HGA are not simple subjective consequences of dissociation, but really reduce pain transmission and reflex arc.

PP.09.12 RENAL SYMPATHETIC DENERVATION IMPROVES GLUCOSE METABOLISM THROUGH AN ACTIVATION OF SODIUM DEPENDENT GLUCOSE TRANSPORTER 2 IN TYPE 2 DIABETIC RATS

A. Nishiyama [1], Y. Fujisawa [1], A. Rahman [1], M. Mogi [2], A. Sufiun [1], K. Rafiq [1] *[1] Kagawa University, Kagawa, JAPAN, [2] Ehime Universiy, Matsuyama, JAPAN*

Objective: Recent studies have shown that renal sympathetic denervation (RDX) improves glucose metabolism in patients with resistant hypertension.

However, the mechanisms underlying the beneficial effects of RDX are poorly understood. Here, we examined the effects of RDX at diabetic stage on glucose metabolism in type 2 diabetic rats.

Design and method: Otsuka Long Evans Tokushima Fatty (OLETF) rats were underwent uninephrectomy and RDX at 5 and 25 weeks of age, respectively. Blood pressure was measured by telemetry system.

Results: At 45 weeks of age, RDX animals had almost undetectable renal cortical tissues norepinephrine (NE) levels. RDX-OLETF rats showed lower levels of blood glucose, plasma insulin and their area under the curve in response to oral glucose loading during the oral glucose tolerance test, as compared to non denervated rats. Furthermore, the whole body insulin sensitivity was assessed by the hyperinsulinemic-euglycemic clamp study at 45 week of age, and RDX-OLETF rats showed an improved glucose infusion rate, as compared to non denervated rats. RDX suppressed plasma and renal tissues NE levels, lowered urine NE excretion, and improved in vivo glucose uptake by adipose tissues, soleus muscle and liver tissues in OLEFT rats. Furthermore, RDX markedly increased urinary excretion rate of glucose which was associated with a decrease in sodium dependent glucose transporter 2 (SGLT2) expression in proximal tubular brush border membrane.

Conclusions: These data suggest that renal sympathetic denervation improves glucose metabolism by increasing glucose uptake at peripheral tissues and urinary glucose excretion.

PP.09.13 INADEQUATE BLOOD PRESSURE CONTROL IN HYPERTENSIVE PATIENTS RECEIVING ANTIHYPERTENSIVE THERAPY IS ASSOCIATED WITH AUTONOMIC DYSFUNCTION

O. Mamontov [1], I. Brodscaya [2], E. Shlyakhto [1]. *[1] Almasov Federal Center of Heart Blood and Endocrinology, Saint-Petersburg, RUSSIA, [2] The first Saint-Petersburg State Medical University, Acad. Pavlov, Saint-Petersburg, RUSSIA*

Objective: Inadequate blood pressure (BP) control, which may influence the difficulty selection of antihypertensive therapy (AHT) can be associated with impaired neurogenic control of blood circulation.
Aim. To study features of autonomic control circulation in patients with arterial hypertension (AH), which had different variants disorders BP profile despite AHT.

Design and method: Study included 106 patients with arterial hypertension (AH) treated with combination AHT, mean age 54,8±6,1 years. 72 patients had associated cardiovascular disease (CHD, stroke and diabetes).
All patients were performed ambulatory BP monitoring (BPLab, Russia) and study of autonomic regulation: tilt-test (TT), Valsalva maneuver, assessment dynamics forearm blood flow (DFBF) during lower body negative pressure (LBNP) -10 mmHg, arterial baroreflex (BRS), heart rate variability (HRV), blood pressure variability (VAD) and cross-spectrum. Hemodynamic parameters recorded using beat-to-beat BP monitor (Finometer-PRO, Nederland), occlusion plethysmography and ECG.

Results: During ambulatory monitoring revealed that 51 patients not been achieved adequate control blood pressure profile. It caused an increase BP during the day in 17, at night - 31 patients; increase diurnal blood pressure variability (DVAD) in 33, inadequate blood pressure reduction at night in 24 patients. DBF during LBNP was lower in patients with high daily systolic BP (SBP) (–0,11±0,10vs. 0,30±0,20 RU; p<0,05) and at night (–0,06±0,15vs.0,33±0,24 RU; p<0,01). BRS correlated with daily SBP (r=–0,28; p<0,05), DFBF during LBNP correlated with daily SBP (r=–0,47; p<0,01) and at night (r=–0,63; p<0,001). Diurnally diastolic BP (DBP) associated with HRV, BPV and cross-spectrum, notably in low frequency range (r=0,38; p<0,01, r=0,29; p<0,01, r=0,40; p<0,005, respectively). Patients with high DBP more significantly decreased SBP in orthostasis (-12,5±12,5 vs. -0,3±11,2 mm Hg; p <0,01). In patients with elevated DVAD were observed decrease the Valsalva index (1,49±0,21 and 1,73±0,24; p<0,01) and orthostatic hypertension (x2=4,4; p <0,05). Patients with inadequate night decrease SAD or DBP had less BRS (6,1±3,0 vs. 9,5±5.3 ms/mmHg; p<0,05) and DFBF during LBNP (0,01±0,18 vs. 0,36±0,25 RU; p<0,05).

Conclusions: In patients with resistance to AHT and various disorders of blood pressure profile observed different types autonomic dysfunction, which can lead to difficulties in selection adequate treatment.

PP.09.14 CAROTID CHEMO- AND BARORECEPTORS IN OBESITY HYPERTENSION

T. Lohmeier [1], D. Georgakopoulos [2], E. Irwin [3]. *[1] Univ. of Mississippi Medical Center, Jackson,MS, USA, [2] CVRx, Inc., Minneapolis,MN, USA, [3] North Memorial Medical Center, Robbinsdale, MN, USA*

Objective: Carotid bodies (CB) influence sympathetic activity, and the peripheral chemoreflex is enhanced in both human and experimental hypertension (HT). We hypothesized that activation of carotid chemoreceptors contributes to sympathetically-mediated obesity-induced HT. In dogs with obesity HT (n=4), antihypertensive responses to CB denervation were compared to responses during chronic electrical activation of the carotid baroreflex (BA), which has sustained effects to suppresses central sympathetic outflow.

Design and method: After baseline hemodynamics were recorded at normal body weight, the diet was supplemented with beef fat, whereas Na intake was held constant. After 5 weeks on the high-fat diet (obese), when body weight had increased ~40%, fat intake was reduced to a level that maintained this body weight. Responses to 1 week of BA (week 6) were recorded followed by 1 week of recovery (week 7). The carotid sinuses were then denervated (CSD), and 2 weeks of hemodynamic data were recorded.

Results: Weight gain resulted in increased mean arterial pressure (MAP) and substantial increases in heart rate (HR). MAP decreased within 5 days of CSD and continued to fall until the severity of HT was attenuated ~ 40% (week 9). During this time, there were no significant changes in HR. In contrast, BA completely abolished the HT within 24 hours of electrical stimulation of the carotid sinus and greatly diminished the tachycardia by improving vagosympathetic balance. CSD abolished ventilatory responses to IV injection of NaCN and led to a sustained increase in arterial PCO2 (39±1 to 53±1 mmHg), indicating successful CB denervation.

Condition	MAP (mmHg)	HR (bpm)
Lean	103±2*	82±3*
Obese (week 5)	123±4	115±2
BA (week 6)	103±2*	97±4*
Recovery (week 7)	125±2	117±3
CSD (week 9)	116±3*	112±5

P< 0.05 vs Obese (week 5)

Conclusions: These findings suggest that CB are active in obesity and contribute to the sympathetically-mediated HT, but that their influence on MAP can be counteracted by BA. Because intermittent hypoxia increases the chemosensory response of the CB and because obstructive sleep apnea is prevalent in obesity, this neurogenic mechanism may be especially important in mediating human obesity HT. HL-51971.

PP.09.15 FAILURE IN PARASYMPATHETIC MODULATION AND VASCULAR REMODELING: AN ASSOCIATION INDEPENDENT OF BLOOD PRESSURE AND AGING IN HYPERTENSIVE PATIENTS

S. González, M. Casarini, F. Inserra, E. Cavanagh, C. Castellaro, P. Kempny, J. Chiabaut Svane, S. Obregon, A. Hita, C. Kotliar. *Hospital Universitario Austral, Derqui, ARGENTINA*

Objective: Diverse factors have been associated with vascular remodeling (VR), primarily aging and hypertension. Abnormal autonomic regulation, which is involved in different pathophysiological pathways of cardiovascular disease, could impact on VR beyond the above factors.
To assess: a) the associations between autonomic profile and VR. b) Whether autonomic variables are independent predictors of VR.

Design and method: 300 consecutive patients were evaluated (March/2012–October/2013). After exclusion criteria (cardio/renal-diseases, anemia, β-blocker-therapy, antidepressants, antiarrhythmics, bronchodilators), 171 patients remained: 89 treated-hypertensives (52.0±11.1 years, 141.1±11.6/89.1±9.70 mm Hg, 87.6% males) and 82 normotensives (47.0±9.53 years, 119.0±10.0/76.5±8.31 mm Hg, 70.1% males). Anthropometry, resting BP (OMROM HEM781), carotid-femoral atherosclerosis and common-carotid intima-media thickness (CIMT; Esaote My Lab 40) were evaluated. Autonomic balance was measured through heart rate variability at rest (5 min). Parasympathetic modulation in time-domain (RMSSD) and sympathetic tone in frequency-domain (Low-High frequency (Lf/Hf), by autoregressive method) were determined. VR was defined as maximum CIMT>0.90 mm and/or plaque. In hypertensive and normotensive patients, univariate correlations were performed between logarithmically normalized RMSSD and Lf/Hf and maximum CIMT (Pearson). Mean-difference analyses of RMSSD and Lf-Hf according to presence/absence of atherosclerotic plaque (T Test) were done. Logistic regression was performed with VR as dependent variable.

Results: In hypertensives, RMSSD and Lf/Hf correlated inversely and directly, respectively, with maximum CIMT (r= -0.41, p<0.001 and r=0.24, p=0.02). Plaque presence was associated with lower parasympathetic (RMSSD: 18.4ms vs. 27.4ms, p<0.002) and higher sympathetic (Lf/Hf: 2.51 vs 1.70, p = 0.04) modulations. In normotensives no significant associations between autonomic profile and maximum CIMT or plaque presence were found (p>0.05 in all cases). In logistic regression, age and RMSSD were independent predictors of VR (adjusted for sex, smoking, SBP, diabetes and BMI; p=0.002 and p=0.04, respectively).

Variable	Coefficient	Std. Error	P
Age	0,1353	0,04376	0,0020
Male sex	-1,5775	1,0555	0,1350
Smoker	0,2160	0,9153	0,8134
BMI	-0,01165	0,07301	0,8732
SBP	-0,003782	0,02159	0,8610
Diabetes	-0,8555	1,3282	0,5195
RMSSD	-1,9010	0,9271	0,0403
LfHfar	0,1502	0,2132	0,4809
Constant	2,3578		

Conclusions: In hypertensive, but not in normotensive patients, a lower parasympathetic modulation was associated with VR beyond age and BP values. Sympathetic tone showed no independent association with VR in this study. Thus, future investigations will be needed to evaluate if an impaired vagal modulation, through specific mechanisms (i.e: inhibition of vagal anti-inflammatory reflex), could be linked to VR in essential hypertension.

PP.09.16 BARORECEPTOR STIMULATION ENHANCED NO-DEPENDENT VASCULAR DILATION, A NEW TREATMENT FOR ARTERIAL HYPERTENSION AND METABOLIC SYNDROME

J. Gmitrov [1,2,3]. [1] *National Institute of Public Health, Department of Environmental Health, Tokyo, JAPAN,* [2] *Pro Vitae Hospital, Diabetology Clinic, Gelnica, SLOVAK REPUBLIK,* [3] *Krompachy Hospital, Diabetology Clinic, Krompachy, SLOVAK REPUBLIK*

Objective: Increasing evidence suggests nitric oxide (NO) deficit and baroreflex dysfunction to be characteristic for cardiovascular conditions even in preclinical stages of the disease. Sodium nitroprusside (SNP), a spontaneous NO-donor, vasodilatory effect was studied in conjunction with sinocarotid baroreceptor magnetic stimulation and potential implementation in cardiovascular conditions with autonomic dysfunction and NO deficit.

Design and method: Mean femoral artery blood pressure (MAP), heart rate (HR) and ear lobe skin microcirculatory blood flow, measured by microphotoelectric plethysmogram (MPPG) were simultaneously recorded in conscious rabbits before and after 40-min local exposure of sinocarotid baroreceptors to 350 mT intensity static magnetic field (SMF), generated by Nd-Fe-B alloy magnets (n = 14) or sham magnets (n = 10, controls). Arterial baroreflex sensitivity (BRS) was measured by the changes in HR and MAP after intravenous (i.v.) bolus injections of SNP and phenylephrine.

Results: SMF significantly decreased systemic MAP (-6.2%), phenylephrine-induced abrupt elevation in MAP (-21.9%) and increased microcirculatory blood flow (+23.0%), and BRS (+68.8). An increase in BRS significantly correlated with decrease in phenylephrine MAP ramps ($r = -0.47$, $p < 0.016$) and increase in microcirculatory blood flow ($r = 0.66$, $p = 0.009$), indicating improvement of the baroreflex-mediated makro- and microcirculatory control. The microvascular vasodilatory response due to same dose i.v. bolus of nitroprusside significantly increased after SMF exposure (+163.2%) and significantly correlated with increase in BRS ($r = 0.56$, $p = 0.021$).

Conclusions: A larger vasodilatory effect of a sodium nitroprusside (NO-donor) on the background of increased BRS suggests augmentation of the baroreflex capacity support NO-dependent vasodilation to be a new physiological mechanism of blood pressure buffering and microcirculatory control. Baroreceptor magnetic stimulation, improving microvessels sensitivity to NO, could augment insulin-mediated skeletal muscle vasodilation (which is NO-dependent), nutritive blood flow and glucose uptake, ameliorating insulin resistance and the metabolic syndrome. Baroreceptor stimulation seems to be a new complex systemic approach how to stabilize enhanced blood pressure variability, moderate autonomic, vascular and endothelial dysfunction with potential implementation in an array of cardiovascular and metabolic diseases where NO deficit and autonomic dysfunction increases the risk of morbidity and mortality substantially.

PP.09.17 SYMPTOMS RECURRENCE IN PATIENTS WITH POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME

J. Freitas, A. Sousa, A. Lebreiro, R. Santos, M. Maciel
Centro Hospitalar Sao Joao, Porto, PORTUGAL

Objective: Postural orthostatic tachycardia syndrome (POTS) is defined as the development of orthostatic symptoms with a heart rate increment >= 30. POTS's clinical presentation and its pathophysiology are complex. The prognosis of this condition remains uncertain and limited data is available regarding long-term symptoms recurrence.

Design and method: We retrospectively analyzed clinical records of pts with POTS diagnosed, from January 2000 to December 2010. Demographic data, comorbidities and symptoms were analyzed. A follow-up (FUP) survey was conducted in December 2012. Pts without FUP data were excluded.

Results: A total of 19 pts were included, all women, mean age 27.4 ± 8.9 years. Mean FUP time was 92±41 months. Overall, on FUP, five pts (31.3%) were asymptomatic, 9 (56.3%) improved significantly their quality of life but two pts (12,5%) remained highly symptomatic. Patients were divided according to their symptomatic status on FUP into 2 groups: highly symptomatic patients versus assymptomatic or midly symptomatic patients.
There were inter-group differences referring to age, symptom pattern (syncope, dizziness, visual symptoms, diaphoresis, palpitations, pallor, headache, nausea, asthenia, chest pain, dyspnea, tremor, heat intolerance, diarrhea) , as well as the postural context (orthostatic symptoms only vs sitting position symptoms also vs supine symptoms also). Higher frequency of dyspnea and headache during the episodes and occurrence of supine symptoms were associated with a higher probability of symptoms recurrence on FUP ($p<0,05$ for all analysis).

Conclusions: Simple clinical data (symptoms and their context) may be of value in symptoms recurrence preview, an important determinant of quality of life in pts with POTS.

PP.09.18 VASCULAR ULTRASOUND DETERMINANTS OF BRAIN INFARCTION IN HYPERTENSIVE DIABETIC PATIENTS

G. Dimas [1], T. Tegos [2], F. Iliadis [1], I. Kanellos [1], S. Fotiadis [1], M. Apostolopoulou [1], G. Konstantinidis [1], I. Chrysogonidis [3], E. Liouta [1], C. Savopoulos [1], A. Hatzitolios [1]. [1] *First Propaedeutic Medical Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE,* [2] *First Neurology Medical Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE,* [3] *Radiology Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE*

Objective: It has been demonstrated that the ultrasound findings of carotid arteries are associated with ischemia on cerebral imaging. In an effort to better determine the impact of the atherosclerotic load on brain parenchyma, a study was performed aiming to establish the association of carotid and femoral ultrasound findings with ischemia on brain computerised tomography (CT).

Design and method: Analysis involved imaging by duplex of carotid and femoral arteries of 74 hypertensive diabetic patients (46 male and 28 female, mean age: 64.29 years) in longitudinal fashion, to detect the presence of plaque and to assess the intima-media thickness (IMT). Each artery was assigned a score (presence of plaque= 1, absence of plaque=0, IMT>0.8 mm=l, IMT<0.8 mm=0) and the total score of the four vessels (two carotids and two femorals) was calculated per patient (atherosclerotic ultrasonic score-ATHUS). Subsequently, brain CT scans were performed in all patients and the presence or absence of ischemia was noted.

Results: Group A (ATHUS=0-2, 26 patients) was associated with a 19.2% (5/26) prevalence of brain CT ischemia. The corresponding values for group B (ATHUS=3-5, 24 patients) and group C (ATHUS=6-8, 24 patients) were: 45.8% (11/24) and 58.3 %(14/24) respectively ($p<0.05$).

Conclusions: Our results suggested that the degree of atherosclerosis was directly related to brain CT ischemic findings. This position might be clarified in larger studies of patients, aiming to establish the role of atherosclerosis detected on ultrasound in the development of brain CT ischemic findings.

PP.09.19 THE ROLE OF ACETYLCHOLINE INHIBITORS, THYROID FUNCTION AND ATHEROSCLEROSIS IN ELDERLY HYPERTENSIVE PATIENTS WITH VASCULAR DEMENTIA

G. Dimas [1], T. Tegos [2], F. Iliadis [1], I. Kanellos [1], S. Fotiadis [1], M. Apostolopoulou [1], G. Konstantinidis [1], E. Liouta [1], I. Chrysogonidis [3], C. Savopoulos [1], A. Hatzitolios [1]. [1] *First Propaedeutic Medical Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE,* [2] *First Neurology Medical Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE,* [3] *Radiology Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE*

Objective: Atherosclerosis is commonly implied after the findings of carotid ultrasound and lower limp Doppler studies and has also been associated with dementia. Recent studies have shown that patients with vascular dementia (VD) exhibit a cholinergic deficit and they have a good response to treatment with ace-

tylcholinesterase inhibitors (Achl). There is evidence in thyroid mouse models in in vitro studies that achetylocholine stimulates iodine organification without concomitant T4 release. The aim of this study was to assess thyroid function after Achl treatment in VD patients and to investigate its therapeutic impact in patients with VD and impaired atherosclerotic markers.

Design and method: 68 patients who were admitted with diagnosis of stroke and VD were included. As controls there were 50 healthy individuals. The patient group completed a 12 months therapy with Achl (rivastigmine), while the control group received placebo. We investigated changes in thyroid parameters before and after the administration of Achl. Atherosclerotic markers included imaging by duplex of carotid and femoral arteries, has been done before the beginning of Achl treatment and at the completion of the study after 12 months, in order to detect the presence of atherosclerotic plaque and to assess the intima-media thickness IMT),as a calculated marker of subclinical atherosclerosis and subsequently a potential VD. Each artery was assigned a score (presence of plaque=1, absence of plaque=0, IMT>0.8mm-1, IMT<0.8mm-0) and the total score of the 4 vessels (2 carotid and 2 common femoral) was calculated per each patient (atherosclerotic ultrasonic score - ATHUS). Subsequently, the MMSE of every patient was reevaluated.

Results: 12 months after treatment MMSE score was unchanged in 45/50 control individuals and improved in 60/68 patients ($p<0.001$). It seems that Achl benefit patients with VD at least 12 months but not controls. Patients group (ATHUS=3-6, 55 patients) was associated with median MMSE of 27. The corresponding value of the control group (ATHUS= 0-2, 40 persons) was 30 ($p<0.05$)

Conclusions: Our results suggest that Achl treatment has the potential to offer clinical benefit after 12 months of treatment to VD patients who also have evidence of atherosclerotic vascular disease.

PP.09.20 ASSOCIATION OF SERUM LEVELS OF VASCULAR ENDOTHELIAL GROWTH FACTOR-A WITH VASCULAR ULTRASOUND DETERMINANTS OF DEMENTIA IN HYPERTENSIVE PATIENTS WITH TYPE 2 DIABETIC NEPHROPATHY

G. Dimas [1], T. Tegos [2], F. Iliadis [1], I. Kanellos [1], S. Spiroglou [3], S. Fotiadis [1], I. Karamouzis [1], G. Konstantinidis [1], S. Anastasiadou [1], C. Savopoulos [1], A. Hatzitolios [1], D. Grekas [1]. *[1] First Propaedeutic Medical Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE, [2] First Neurology Medical Department, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE, [3] Biochemistry Laboratory, Ahepa University Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE*

Objective: Vascular endothelial growth factor-A (VEGF-A) might play an important role in vessels' remodeling. It remains controversial the mechanism by which VEGF works in the kidney, as well as in the vessels at least in the early stages of diabetic nephropathy (DN) and CKD. Whether VEGF-A is detrimental in early stages of DN or other renal conditions has not yet been clearly answered. Recent evidence supports that combined findings of carotid ultrasound and lower limp Doppler studies denoting atherosclerosis are associated with dementia. VEGF-A may play a role in the pathophysiology of Vascular Dementia (VD). VEGF-A is elevated in postmortem brain tissue of VD patients. VEGF-A has been found in neurons, microglia, vascular endothelial cells and leukocytes. The aim of the present study was to determine the serum levels of VEGF-A and to investigate their potential correlation with the atherosclerotic markers and albuminuria and VD in hypertensive patients with early stages of type 2 DN.

Design and method: CKD patients of stages 1 and 2 with type II DN (n=30) were included. As controls, there were two groups, patients with diabetes type II without CKD (n=15) and healthy individuals (n=15). VEGF-A levels were measured by an ELISA method. Intima media thickness of carotid and femoral arteries and atheromatic plaque were evaluated by a high resolution ultrasonography. Analysis of atherosclerosis markers involved imaging by duplex of carotid and femoral arteries in all patients in longitudinal fashion, to detect the presence of plaque and to assess the intima-media thickness (IMT). Subsequently, the mini-mental score examination (MMSE) of every patient was evaluated.

Results: There was a notable difference between VEGF-A levels in each of the groups.There was a statistically significant correlation between levels of VEGF-A and albuminuria ($p<0.0001$). Further, VEGF-A levels were independently correlated with IMT and atheromatic plaque ($p<0.0001$) and MMSE score in DN patients.

Conclusions: Our study suggests that serum levels of VEGF-A might present independent risk factors of atherosclerosis, albuminuria and vascular dementia in hypertensive patients with early stages of type II diabetic nephropathy to the progression of CKD.

PP.09.21 SELECTIVE CARDIOVASCULAR ADAPTATION TO CHRONIC STRESS IN MICE

P. Davern, B. Abegaz, E.R. Stevenson, K.L. Jackson, C. Gueguen, J. Moretti, G.A. Head. *Baker IDI Heart and Diabetes Institute, Neuropharmacology, Melbourne, AUSTRALIA*

Objective: Exaggerated responses to acute stress and increasing circulating angiotensin II (AngII) contribute to the development of hypertension. While there is habituation with chronic stress leading to less cardiovascular effects, responses to novel stress may be similar or possibly enhanced. In a mouse model of chronic stress, we aimed to investigate cardiovascular responses to repeated and novel stressors and in response to low dose infusion of AngII.

Design and method: Male C57Bl6 mice were implanted with telemetry probes and recordings of mean arterial pressure (MAP) and heart rate (HR) were made in chronically stressed (n=10, 2 hours stress per day for 3 weeks) and in non-stressed (n=4) control mice. Daily stress included a random combination of 60mins of restraint and 2 x 30mins of dirty cage switch and 5mins of shaker stress was chosen as the novel stress. A separate group of non-stressed and chronically stressed mice (n=4 per group) were administered AngII (280µg/kg/day) via minipump and following a final restraint stress, brains were analyzed using immunohistochemistry.

Results: Chronic stress had no effect on basal levels of MAP or HR but attenuated the pressor (14.0 v 21.2mmHg; $P<0.01$) and tachycardic responses (95 v 219bpm; $P<0.001$) to dirty cage switch. Novel shaker stress increased MAP by +7.1mmHg ($P<0.01$) and HR by +70bpm ($P=0.05$) compared with non-stressed mice. No differences were observed in the cardiovascular response to restraint stress. However in AngII infused mice, BP was markedly less in non-stressed mice which was reversed by chronic stress (22.0 v 33.0mmHg; $P<0.05$) and associated with greater Fos labeling in the paraventricular (+11) and dorsomedial (+12) nuclei in the hypothalamus and central (+3) and medial amygdala (+4; all $P<0.05$).

Conclusions: The findings indicate that cardiovascular responses to chronic stressors do not always lead to habituation. Responses to novel stressors can be enhanced and suggests that adaptation to long term stressful situations is non-uniform and may depend on the type of stress involved. Furthermore, the non-uniform adaptation suggests that the modulation likely involves higher brain regions (hypothalamus and amygdala) rather than lower pre-sympathetic pathways.

PP.09.22 ELECTRICAL BAROREFLEX ACTIVATION THERAPY DOES NOT CO-STIMULATE CAROTID BODY CHEMORECEPTORS

E.J.B.M. Goedhart, T. Alnima, P.W. de Leeuw, C.P.M. Van Der Grinten, A.A. Kroon *Maastricht University Medical Centre, Maastricht, NETHERLANDS*

Objective: Carotid baroreflex activation therapy (BAT) by the Rheos® system produces a sustained fall in blood pressure in patients with resistant hypertension. Since the activation electrodes are implanted at the level of the carotid sinus, it is conceivable that the nearby located carotid body chemoreceptors are stimulated as well. Physiological stimulation of carotid chemoreceptors not only raises respiration, but it also increases sympathetic activity which may in part counteract the effects of BAT. The aim of the present study is to investigate whether there is evidence for concomitant carotid chemoreflex activation during BAT.

Design and method: Thirteen participants with the Rheos® system implanted were included in this single-center study. At arrival at the clinic, the device was switched off for 2 hours while patients were at rest. Subsequently, the device was switched on at 6 electrical settings of high and low frequencies and amplitudes. Arterial CO2, end-tidal CO2, breath duration, breathing frequency and blood pressure were measured during all device activation settings. Multilevel statistical models were adjusted for age, gender, blood pressure reduction, antihypertensive medication, sleep apnea, cardiac and lung disease.

Results: Baseline and maximal response end-tidal CO2, PaCO2, breath duration and breathing frequency are presented in Table 1.

TABLE 1: Respiratory and blood pressure measurements during baseline (device off) and the maximum tolerable electrical activation

Device Settings	$PaCO_2$	$ETCO_2$	BD	BF	MAP
Device off	5.75±0.41	4.70±0.54	3.56±0.62	17.91±2.76	103±17
Max activation	5.77±0.43	4.63±0.52	3.61±0.51	17.62±2.37	95±22 *

*Values are in mean ± SD. Max activation = maximum tolerable electrical activation; $PaCO_2$ = arterial CO_2 (kPa); $ET\ CO_2$ = end-tidal CO_2 (kPa); BD = breath duration (seconds); BF = breathing frequency (breaths/minute); MAP = mean arterial pressure (mmHg). * $P < 0.05$ vs baseline.*

These values did not change significantly during any of the electrical settings. Nevertheless, mean arterial pressure showed a highly significant decrease during electrical activation (P<0.001).

Conclusions: Carotid BAT using the Rheos® system did not result in raised respiratory activity at maximally tolerated settings, which suggests that co-activation of carotid body chemoreceptors does not occur during BAT.

PP.09.23 CAROTID SINUS MASSAGE: A POTENTIAL TOOL FOR SELECTING SIDE FOR DELIVERING BAROREFLEX ACTIVATION THERAPY IN PATIENTS WITH RESISTANT HYPERTENSION

T. Alnima, P.W. de Leeuw, A.A. Kroon
Maastricht University Medical Centre, Maastricht, NETHERLANDS

Objective: Carotid baroreflex activation therapy (BAT) is a renewed therapy to treat resistant hypertension. Currently, the activation electrodes are implanted only unilateral, preferably at the right carotid sinus. The aim of this study is to assess the side dominance of carotid baroreflexes in hypertensive patients and to evaluate the use of carotid sinus massage (CSM) to predict the best carotid sinus side to deliver BAT before surgical implantation.

Design and method: To this aim we studied 18 patients that were already implanted bilaterally and, currently receiving BAT. CSM was performed twice at each sinus in a random order. The greatest reflex side was determined when the difference between left and right blood pressure and heart rate drop was >5 mmHg and >=3 beats per minute, respectively. The strongest reflex during CSM was retrospectively compared to the strongest baroreflex side during routine testing with the BAT-system.

Results: Mean decrease in systolic blood pressure was 30 ± 13 and 22 ± 11 mmHg after right and left CSM, respectively (p=0.015), whereas heart rate dropped by 21 ± 10 and 12 ± 8 bpm, respectively (p=0.001). 89% of patients had a larger effect of CSM at the right side. The same trend was observed during BAT and the proportions of left/right dominance were equal between CSM and BAT.

Conclusions: Carotid baroreflexes in hypertensive patients show side-dominance towards the right sinus. Nevertheless, a minority of patients had a greater left-sided baroreflex. Therefore, it may be worthwile to consider performing CSM in candidate patients before implanting BAT unilaterally.

PP.09.24 NITRIC OXIDE SYSTEM INHIBITION MODIFIES CARDIAC AQP1 LOCALIZATION DURING HYPOVOLEMIC STATE IN GROWING RATS

V. Netti, A. Iovane, L. Alencastro, E. Zotta, A. Fellet, A.M. Balaszczuk
Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, IQUIMEFA-CONICET, Buenos Aires, ARGENTINA

Objective: We previously showed that cardiac AQP1 is altered during hypovolemic state according to the stage of postnatal growth studied. Considering that it has been reported that AQP1 facilitates nitric oxide (NO) transport across the plasma membrane, the objective of the present work was to study if NO system inhibition regulates AQP1 in vivo during water restriction in cardiac tissue of 25-day-old pups.

Design and method: Male Sprague-Dawley rats aged 25 days were randomly assigned as follows (n = 7 each group): R: water restriction during 3 days; C: water ad libitum for 3 days; RL: infusion of L-NAME (4mg/kg.day) via ALZET osmotic mini pumps + water restriction during 3 days; CL: infusion of L-NAME (4mg/kg.day) + water ad libitum for 3 days. At the end of each experimental period, we determined cardiac weight and water content (according to Ding et al.), cardiomyocyte mean diameter and AQP1 localization by immunohistochemistry and protein levels by Western Blot.

Results:

	C	CL	R	RL
Body Weight (g)	85 ± 10	90 ± 7	56 ± 6*	57 ± 6*
Hematocrit (%)	42 ± 2	43 ± 2	55 ± 3*	54 ± 2*
Heart weight (g)	0,47 ± 0,08	0,46 ± 0,05	0,35 ± 0,06*	0,33 ± 0,04*
Cardiomyocyte diameter (μm)	15,0 ± 1,7	15,4 ± 1,9	13,0 ± 1,4*	15,1 ± 1,6#
Cardiac water content (%)	91,7 ± 0,4	92,9 ± 1,6	87,6 ± 0,4*	95,2 ± 1,2#

*p<0.05 vs. C group; #p<0.05 vs. R group

In order to verify NO system inhibition, NOS activity was measured in cardiac tissue of all groups of animals. CL and RL groups presented decreased NOS activity by 50% after L-NAME treatment, in comparison to C group. AQP1 immmunostaining showed the presence of this water channel in the endothelium and endocardium in all groups of animals, being this pattern unchanged by water restriction. However, in animals of RL group, it was observed that AQP1 was present in cardiomyocyte plasma membrane. Cardiac AQP1 protein levels did not change after water restriction or L-NAME treatment in the experimental groups studied.

Conclusions: Water restriction induced a decrease in cardiomyocyte mean diameter and water content, associated to unchanged AQP1 protein levels or localization. L-NAME treatment during hypovolemic state induced the appearance of AQP1 in the plasma membrane, associated to a larger mean cardiomyocyte diameter and cardiac water content, similar to control group. Therefore, NO system inhibition modifies cardiac AQP1 localization and improves cardiac water balance during hypovolemic state in early stages of postnatal life.

PP.09.25 SODIUM-DEPENDENT ION-EXCHANGE SYSTEM IN ITS ROLE AS THE PRIMARY TARGET GASOTRANSMITTERS IN CONTRACTILE REACTIONS OF SMOOTH MUSCLE CELLS

I. Kovalev [1], S. Gusakova [1], T. Idamgapova [1], J. Birulina [1], D. Marchik [1], A. Marchenko [1], D. Nosov [1], L. Smagliy [1], A. Popov [2], M. Medvedev [3], S. Orlov [4].
[1] Siberian State Medical University, Department of Biophysics and Functional Diagnostics, Tomsk, RUSSIA, [2] Siberian State Medical University, Department of Physiology, Tomsk, RUSSIA, [3] M.V. Lomonosov Moscow State University, Department of Biology, Moscow, RUSSIA, [4] M.V. Lomonosov Moscow State University, Department of Biology, Moscow, RUSSIA.

Objective: It becomes increasingly evident that the traditional alarm systems of smooth muscle cells (calcium ions, cyclic nucleotides, the decay products of phosphoinositides and proteinkinase C), you must attach gas transmitters (NO, H2S, CO). Confirms the legitimacy of such an approach involving them in processes of intra-and intercellular communication, as well as participation in the development of pathogenesis of a large number of cell dysfunctions. However, the different steps of gas transmitters can be explained not only by their influence on these processes, and/or involvement in the operation of various intracellular effector systems.

Design and method: Using the double sucrose bridge was studied the influence of the gas transmitters electrical and contractile activity of smooth muscle cells of the ureter Guinea pig caused by an electrical stimulus. Participation in the studied processes Na/H- exchanger and Na,K,2Cl-cotrasporter avoiding the use of inhibitors ethylisopropilamiloride (1 μM) and bumetanide (100 μM microns), respectively.

Results: It is shown that application of inhibitors of Na/H exchanger / Na,K,2Cl-cotrasporter and free-Na solutions reduces the severity of contractile reactions NO, H2S, CO, at a concentration of 100 μM.

Conclusions: Thus, miogenic action gasotransmitters on smooth muscles due to preferential activation Na/H exchanger and Na,K,2Cl- cotrasporter.

PP.09.26 AGE RELATED AQUAPORIN-1 CHANGES ARE ASSOCIATED TO CARDIAC WATER HOMEOSTASIS DURING DEHIDRATION

A. Iovane, V. Netti, L. Alencastro, E. Zotta, A. Fellet, A.M. Balaszczuk
Cátedra de Fisiología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, IQUIMEFA-CONICET, Buenos Aires, ARGENTINA

Objective: Water channel aquaporin-1 (AQP1) is involved in the maintenance of cellular osmotic environment. Even though this protein has been linked to cardiovascular homeostasis, its physiological role still remains to be explored, particularly in the postnatal period. The aim of the present study was to evaluate cardiac AQP1 in rats subjected to hypovolemic state following water restriction during the growth stage.

Design and method: Male Sprague-Dowley rats aged 25 and 50 days were divided in the following groups: R: water restriction during 3 days; C: water ad libitum for 3 days. At the end of each experiment, we determined: cardiac weight and water content (according to Ding et al.), cardiomyocyte mean diameter, cardiac fibrosis (Trichrome staining) and AQP1 protein levels (Western Blot) and localization (Immunohistochemistry).

Results:

	C25	R25	C50	R50
Body weight (g)	83 ± 10	52 ± 6*	240 ± 12†	179 ± 10*
Heart weight (g)	0,46 ± 0,07	0,34 ± 0,08*	0,83 ± 0,13†	0,73 ± 0,09
Heart weight (g/100g)	0,49 ± 0,04	0,48 ± 0,06	0,35 ± 0,04†	0,38 ± 0,05
Cardiac water content (%)	91,7 ± 0,4	87,6 ± 0,4*	91,5 ± 0,7	91,2 ± 0,6
Cardiomyocyte mean diameter (μm)	15,4 ± 0,3	12,1 ± 0,2*	17,2 ± 0,4†	16,3 ± 0,3

*p<0.05 vs. respective C; †p<0.05 vs. 25-day-old rats

Cardiac tissue stained with Masson's trichrome did not show increased fibrosis in neither of the experimental groups. AQP1 immunohistochemical staining of the heart revealed its presence in vascular endothelium and endocardium in control animals of both age groups. No changes in AQP1 localization or protein levels were observed in the 25-day-old group submitted to water restriction.

In the oldest group, AQP1 staining appeared in the plasma membrane and its protein levels were increased in response to water restriction.

Conclusions: Water restriction protocol induced a decrease in heart weight, cardiac water content and cardiomyocyte mean diameter without fibrosis development in the 25-day-old rats; such results may be compatible with microcardia. Increased AQP1 protein levels and membrane localization in the 50-day-old group may prevent such alterations, probably indicating that AQP1 participates in maintaining cardiac water homeostasis during hypovolemic state in mature rats.

PP.09.27 CYSTEIN-RICH ANGIOGENIC PROTEIN 61 PROMOTES VASCULAR SMOOTH MUSCLE CELL CALCIFICATION VIA METALLOPROTEINASE ACTIVATION

H. Lee [1], B. Oh. [1] *Seoul National University Hospital, Seoul, SOUTH KOREA*

Objective: Cystein-rich angiogenic protein 61 (CYR61, CCN1) was reported to be regulated by angiotensin II in vascular smooth muscle cells (SMCs) of atheromatous plaque. Because CYR61 was reported to induce osteoblastic differentiation of mesenchymal stem cells, we hypothesized that the CYR61 may play a role in vascular calcification.

Design and method: We performed experiments using vascular smooth muscle cells harvested from mouse thoracic aorta. We screened global gene expression after CYR61 adenoviral transfection. We evaluated vascular smooth muscle calcification by the expression of osteoblast master transcription factor, Runx2, alkaline phosphatase activity assay and Von Kossa stain.

Results: CYR61 expression was induced by 20.3 folds in SMCs harvested from thoracic aortas of male C57BL6 mouse after 16 hours of adenoviral vector (Ad-CYR61, 50 MOI) transfection, which significantly induced SMC calcification by 209.5±54.8% evaluated by Von Kossa staining after 14 days. In order to evaluate the full range of effects of CYR61 on SMC calcification, we performed microarray analysis. Several metalloproteinases such as MMP-13, -3, -10, and -8 were induced by 55.3, 49.9, 6.4 and 5.2 folds, whereas tissue inhibitor of metalloproteinases such as TIMP-3 and -2 were reduced by 52% and 31% after 16 hours of Ad-CYR61 transfection, respectively (all $p<0.05$). Remarkably, we found overall suppression of procollagen gene expression. Real time PCR confirmed MMP-13 gene induction by 33±13 folds compared with control adenovirus transfected SMCs ($p<0.05$). Although mRNA or protein expressions of MMP-9 were not found increased, gelatin zymography showed an increased enzymatic activity of MMP-9 (92kDa) by 20241% by Ad-CYR61, which was completely reversed by MMP-13 siRNA. Inhibition of MMP activity by the global MMP inhibitor, doxycycline completely blocked Ad-CYR61-induced calcification to the 87.0±30.8% of the control adenovirus transfected SMCs. Also, Ad-CYR61 failed to induce calcification in VSMCs harvested from MMP-9 knock out mouse (100.9±7.6% of the control adenovirus transfected SMCs, $p=0.90$).

Conclusions: These findings demonstrate that CYR61 induces SMC calcification through MMP-13 - MMP-9 cascade. Therapies targeting this signaling pathway may regulate vascular calcification.