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# P.048: AORTIC SYSTOLIC BLOOD PRESSURE: ESTIMATION FROM THE POINT OF SYSTOLIC AUGMENTATION IN THE DIGITAL ARTERY WAVEFORM

S.M. Munir\*, A.Y. Guilcher, B. Clapp, S. Redwood, P.J. Chowienczyk

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PVF and WSS, relative differences of  $6\pm8\%$  (p<0.05) and  $-1\pm15\%$  (p<1) respectively were evidentiated. The estimations based on Poiseuille theory present a significant underestimation of both maximum and mean PVF as well as maximum WSS by comparison to the results obtained through Womersley profiles fitting. No significant difference was observed for the mean WSS.

## P.044 ROLE OF INTEGRIN $\alpha 1\beta 1$ in the Cardiovascular effects of angiotensin ii

H. Louis<sup>1</sup>\*, D. Rouy<sup>2</sup>, A. Kakou<sup>1</sup>, Z. Li<sup>3</sup>, C. Labat<sup>1</sup>, H. Gardner<sup>4</sup>, D. Wagner<sup>2</sup>, P. Lacolley<sup>1</sup>. <sup>1</sup>Inserm U684, Vandoeuvre les Nancy, France, <sup>2</sup>Cardiovascular Research Laboratory CRP-Santé, Luxembourg, Luxembourg, <sup>3</sup>UMR7079, University Paris 6, Paris, France, <sup>4</sup>Department of Research Pathology, Biogen Idec, Cambridge, United States

Integrin  $\alpha 1$  knockout mice ( $\alpha 1$ -/-) were used to investigate the role of the integrin  $\alpha 1\beta 1$  in the cardiac and vascular functions of angiotensin II (AngII)-induced hypertension. Carotid artery (CA) elasticity was measured by incremental elastic modulus (Einc)-wall stress curves using an ultrasonic echo-tracking device and the measurement of medial cross-sectional area (MCSA) to evaluate  $in\ vivo\ CA$  mechanical properties. Cardiac function was studied by echocardiography in anaesthetized animals.

Infusion of Ang II (200ng/kg/min) in  $\alpha$ 1-/- mice and their control ( $\alpha$ 1+/+) for 4 weeks led to similar hypertensive effect (SAP +31 vs +37 mmHg). In  $\alpha$ 1-/- Ang II failed to increase MCSA of CA whereas it did in  $\alpha$ 1+/+ mice. The Einc-stress curve of Ang II-treated  $\alpha$ 1-/- was shifted to the right compared to Ang II-treated  $\alpha$ 1+/+, indicating a decreased arterial stiffness. The  $\alpha$ 1+/+ had an increased cardiac hypertrophy, evaluated by an increase of the end diastolic thickness of the septum (IVSd: 1.2±1 vs 0.9±0.08 mm) without modification of the posterior wall (LVPWd: 0.10±0.6 vs 0.97±0.07 mm) and without dilation of the ventricular cavity. This septal hypertrophy was not found in the  $\alpha$ 1-/- mice in response to Ang II. Cardiac fibrosis measured by collagen quantification (total, and type I and III), was lower in the  $\alpha$ 1-/- mice, compared with the  $\alpha$ 1+/+.

In conclusion, our results show an impaired of cardiovascular response to Ang II-induced hypertension in the integrin  $\alpha 1$  knockout mouse. These results suggest the involvement of this integrin in the cardiovascular effects of Ang II.

#### P.045

## STABLE THE REFLECTIVE PROPERTIES OF THE ARTERIAL SYSTEM IN RENAL TRANSPLANTATION (RTX) PATIENTS AT ONE YEAR FOLLOW-UP

N.G. Mardare\*, P. Gusbeth-Tatomir, A. Covic. 'Dr. CI Prahon' University Hospital, Dialysis and Transplantation Center, Iasi, Romania

**Background:** Successful RTx from living-related donors, by removal of the uremic milieu and improvement in cardiovascular risk factors can be associated with improvement in indices of arterial stiffness. The aim of this study was to assess the arterial stiffness after one year of follow-up in live related RTx patients.

**Methods:** The augmentation index (Alx) was determined from arterial waveforms contour analysis recorded by applanation tonometry using SphygmoCor® device in 31 living related RTx (19 M, age 34.6±8.5 yrs; RTx duration 29.7±24.8 Mo, mean Cr.Cl. = 69.2±1.2 ml/min). All studies were performed before CsA administration, at baseline and at one-year follow-up. As a surrogate marker of the pulse wave velocity (PWV) we used the time to shoulder (TTS) parameter on the reconstructed central pulse pressure contour wave.

Results: Overall, during follow-up, mean Alx increased from  $13.5\pm13.3\%$  to  $15.6\pm10.5\%$  (p=NS). TTS increased from  $107.7\pm9.5$  ms at baseline to  $109.3\pm9.5$  ms at follow-up (p=NS). Biochemical parameters, blood pressure and heart rate remained unchanged over the follow-up period. On univariate analysis, at both moments, Alx and TTS correlated with anthropometric parameters (height and weight) and serum creatinine (independent predictor at baseline  $R^2 = 0.443$ ; p < 0.05). There was no correlation of the arterial stiffness parameters with creatinine clearance or CsA therapy (dosage/levels).

**Conclusions:** In our study we demonstrate that there are no significant overall changes in arterial stiffness properties after one-year follow-up in stable renal transplant patients.

## P.046 INSIGHTS FROM PULSE WAVE VELOCITY ACROSS CONTRASTING DISEASES

S. do Vale<sup>2</sup>\*, J. Martin Martins<sup>2</sup>, C. Saldanha<sup>1</sup>, J. Martins e Silva<sup>1</sup>. <sup>1</sup>Chemical Biopathology Institute, Lisbon Medical School, Lisbon, Portugal, <sup>2</sup>Endocrine Department, Santa Maria Hospital, Lisbon, Portugal

**Objectives:** Several disease conditions are associated with an increased risk of vascular events. Direct evaluation of arterial structure and function remains elusive at the clinical level. We now report the results of pulse wave velocity in contrasting diseases.

Patients and Methods: We studied 200 consecutive patients assisted at the out-patient department of a public central hospital: (1) Obesity (OB, n = 60); (2) Type 2 Diabetes Mellitus (DM2, n = 60), Sexual Erectile Dysfunction (SED, n = 80). Patients were compared to controls (C, n = 40). Pulse wave velocity was measured between the carotid-radial arteries (CR) and between the carotid-femoral arteries (CF) with a computerized pressure transducer device (Complior  $^{\circ}$ ).

Results: Compared to controls, values at both sites were significantly increased in every disease condition: CR (m/s): (C)  $7.03\pm1.67$ ; (OB)  $8.21\pm2.08$ ; (DM2)  $8.44\pm3.10$ ; (SED)  $9.63\pm2.10$ ; CF (m/s): (C)  $5.87\pm1.92$ ; (OB)  $7.80\pm2.04$ ; (DM2)  $11.31\pm3.27$ ; (SED)  $13.08\pm4.26$ . CR and CF PWV were directly and significantly related. Higher CR than CF levels were found only in the C group, with no difference in the OB group, and higher CF than CR levels in DM2 and SED groups (p < 0.05). Body volume was a general significant factor for PWV, across diagnostic groups.

Discussion: Non invasive assessment of arterial stiffness by measuring PWV establishes arterial dysfunction in several pathologic conditions associated with an increased cardiovascular risk, even when this is still a matter of debate, namely OB and SED. Increased arterial stiffness is most marked in larger elastic arteries like the aorta (CF-PWV) and reverses the normal PWV gradient against smaller-muscular arteries (CR-PWV).

## P.047 CCR5-DEL32 GENOTYPE MODIFIES PRO-INFLAMMATORY/ /ANTI-INFLAMMATORY CYTOKINE RATIO; POSSIBLE ROLE IN ATHEROGENESIS

H. Moattar\*, G. Foteinos, K. Mandel, B. Zal, A. Weerasinghe, S. Fredricks, M. Jahangiri, N.D. Carter, A. Afzal. *St George's University of London, London, United Kingdom* 

CCR5 is a receptor for several chemokines and is highly expressed on the cells involved in atherogenesis. A 32 bp deletion mutation of CCR5 prevents expression of this molecule on cell surface and is associated with reduced risk of premature coronary artery disease. It was shown that IL-6/IL-10 ratio could be a predictor of further coronary artery events in patients with Non-ST elevation acute coronary syndrome. In the present study we investigated the effect of CCR5-del32 mutation on production of pro-inflammatory and anti-inflammatory cytokines by lymphocytes in basal or stimulated conditions. Subjects were from a cohort of patients admitted to undergo coronary artery bypass graft surgery. Samples from 7 patients who were homozygote for wild type CCR5 allele (CCR5/CCR5) and 7 patients who were heterozygote for CCR5-del32 allele (CCR5/CCR5del32) were used. Peripheral mononuclear cells (PMNC) were separated from whole blood by density gradient centrifugation. The PMNC cultures were either left untreated or incubated with lipopolysaccharide (LPS) or oxidative low density lipoprotein (OxLDL) for 24 hours before collecting their supernatant for cytokines measurement. PMNC carrying del32 produced significantly more IL-6 at baseline and after LPS stimulation. They also produced more IL-10 when stimulated with LPS and OxLDL. However, proinflammatory/anti-inflammatory ratio (IL-6/IL-10 and TNF- $\alpha$ /IL-10) tend to be lower under stimulation by LPS and OxLDL in the group with del32 genotype. We concluded that some aspects of the protective effect of CCR5-del32 mutation against premature atherosclerosis can be attributed to modulation of anti-inflammatory and pro-inflammatory cytokine response in inflammatory cells particularly in PMNC.

#### P.048

## AORTIC SYSTOLIC BLOOD PRESSURE: ESTIMATION FROM THE POINT OF SYSTOLIC AUGMENTATION IN THE DIGITAL ARTERY WAVEFORM

S.M. Munir\*, A.Y. Guilcher, B. Clapp, S. Redwood, P.J. Chowienczyk. Cardiovascular Division, King's College School of Medicine, London, United Kingdom

**Introduction:** Central and peripheral blood pressure and waveforms differ due to effects of wave reflection and amplification. Use of a mathematical transform function to predict central pressure remains controversial. It may be possible to estimate central systolic pressure directly from a peripheral

Poster Presentations \$39

waveform. We investigated this during cardiac catheterisation, examining the effects of pacing and nitroglycerin (NTG) on estimation of central systolic pressure from the peripheral pulse.

Methods: Patients undergoing coronary angioplasty (n = 11, aged 48 to 72 years) participated. A Millar SPC-454D or fluid filled catheter was placed in the aortic root and a pacing wire in the right atrium. Peripheral digital arterial waveforms (Finometer) and aortic waveforms were obtained at baseline, during pacing at 20 bpm above resting heart rate and during administration of NTG (10 and 100 µg/min, i.v.).

**Results:** Pacing and NTG produced marked changes in central and peripheral waveforms, reducing central augmentation index from  $40.4\pm6.2$  to  $22.6\pm8.9\%$  and from  $40.4\pm6.2$  to  $12.7\pm7.0\%$  for pacing and NTG 100  $\mu g/min$  respectively (each P < 0.01). At baseline and during all interventions, there was a close correlation between central systolic blood pressure and absolute finger systolic pressure at the point of late systolic augmentation (R = 0.95, P < 0.0001). The mean difference between measured central aortic systolic BP and that estimated from digital pressure was 2.2 mmHg SD 6.2 mmHg.

**Conclusions:** These data suggest that central systolic blood pressure can be estimated directly from non-invasive finger pressure waveforms even during interventions such as pacing and NTG that produce a marked change in pressure waveforms.

#### P.049

#### EFFECTS OF INHIBITION OF NITRIC OXIDE SYNTHASE ON THE PERIPHERAL ARTERIAL WAVEFORM RESPONSE TO EXERCISE

S.M. Munir\*, B. Jiang, A. Guilcher, S. Brett, S. Redwood, P.J. Chowienczyk. Cardiovascular Division, King's College School of Medicine, London, United Kingdom

**Introduction:** Exercise reduces systolic augmentation in the peripheral pulse wave, an effect similar to that produced by the nitric oxide (NO) donor nitroglycerin (NTG). The changes produced by exercise persist into the recovery period for >30 min. The aim of this study was to investigate if the exercise induced changes are dependent on endothelium-derived NO. We used the NO synthase inhibitor N<sup>G</sup>-monomethyl-L-arginine (L-NMMA) to test this.

Methods: Healthy volunteers (n = 10, 5 female, aged 19 to 33 years) participated in a 2-phase randomised controlled cross-over study. L-NMMA (6 mg/kg i.v. over 5 min) and saline placebo were given immediately before exercise on two occasions separated by at least 5 days. Mean arterial blood pressure (MAP by Finopress), radial augmentation index (RAIx by SphgymoCor) and cardiac output (Innocor) measurements were made at baseline, during infusion of L-NMMA/saline immediately before exercise, during exercise (except for radial artery measurements) and during recovery. Peripheral vascular resistance (PVR) was calculated from MAP and cardiac output. During exercise, workload increased from 25 W to 150 W by increments of 25 W at 2 min intervals.

**Results:** Before exercise, L-NMMA increased mean arterial blood pressure  $(85.1\pm3.8~\text{vs.}~101.2\pm4.3~\text{mmHg},~P<0.01)$ , peripheral vascular resistance  $(16.4\pm0.7~\text{vs.}~24.7\pm1.7~\text{mmHg/ml/min},~P<0.01)$  and RAIx  $(50.2\pm4.5~\text{vs.}~70.2\pm6.5\%,~P<0.01)$  and decreased heart rate  $(65.6\pm5.7~\text{vs.}~49.1\pm2.8~\text{bpm},~P<0.01)$ . During and after exercise, heart rate, MAP and PVR were similar after L-NMMA and saline. However, L-NMMA attenuated the exercise induced fall in RAIx so that RAIx was higher after L-NMMA compared to saline at 15 min in recovery  $(49.5\pm5.3~\text{vs.}~36.0\pm4.4\%,~P<0.02)$ .

**Conclusion:** These data suggest that, although endothelium derived NO has little effect in regulating PVR during/after exercise, it may have a role in mediating exercise induced changes in the pulse waveform.

#### P.050

## THE INSULIN SENSITIZER ROSIGLITAZONE IMPROVES ENDOTHELIAL FUNCTION IN PATIENTS WITH TYPE 2 DIABETES ON INSULIN

K. Papathanassiou<sup>1</sup>\*, K.K. Naka<sup>1</sup>, N. Kazakos<sup>1</sup>, K. Pappas<sup>1</sup>, K. Liveris<sup>1</sup>, D. Makriyiannis<sup>2</sup>, A. Tsatsoulis<sup>3</sup>, L.K. Michalis<sup>1</sup>. <sup>1</sup>Michaelidion Cardiac Center, University of Ioannina, Ioannina, Greece, <sup>2</sup>Department of Endocrinology, Hatzikosta General Hospital, Ioannina, Greece, <sup>3</sup>Department of Endocrinology, University Hospital of Ioannina, Ioannina, Greece

Aim: Thiazolidinediones (TZDs) are insulin sensitizers used to improve glycaemic control in diabetic patients. TZDs have also been reported to improve endothelial function in obese patients with insulin resistance and in diabetic patients on oral treatment. However, little is known about the vascular effects of TZDs in patients with type 2 diabetes treated with insulin. The aim of this study was to assess the effect of rosiglitazone on endothelial function in type 2 diabetic patients treated with insulin.

Methods: Thirty-one diabetic patients without known coronary artery, cerebrovascular or peripheral arterial disease, who were already on an

insulin regime, were randomized into 2 groups; no treatment was added in group A (n=14), while rosiglitazone  $(4\,\text{mg}\ \text{od})$  was added in group B (n=17) for 6 months. Flow-mediated dilation (FMD) in the brachial artery was assessed in all patients, at baseline and at follow-up.

**Results:** At baseline, the 2 groups did not differ in age (mean $\pm$ SD, 67.3 $\pm$ 6.4 vs 64.7 $\pm$ 7.6 years, respectively, p=ns), or any measured variable. In group A there were no significant changes at 6 months in any variable except for diastolic blood pressure that dropped from 79 $\pm$ 7 to 72 $\pm$ 12 mmHg (p < 0.05). In group B, a significant reduction in glycated hemoglobin (from 8.8 $\pm$ 1.1 to 7.8 $\pm$ 1.0%, p < 0.0005) and in fasting plasma glucose (from 186 $\pm$ 64 to 144 $\pm$ 61 mg/dl, p < 0.05) was observed at 6 months, while FMD significantly improved (from 1.43 $\pm$ 1.46 to 2.98 $\pm$ 1.80%, p < 0.005).

**Conclusions:** In insulin-treated type 2 diabetic patients, treatment with rosiglitazone for 6 months has a beneficial effect on glycaemic control and endothelial function.

#### P.05

## EVALUATION OF ENDOTHELIAL FUNCTION WITH NON-INVASIVE METHODS IN DIFFERENT CARDIOVASCULAR DISEASES

J. Nemcsik\*, J. Egresits, J. Borvendég, E. Kolossváry, E. Finta, K. Farkas, I. Kiss. Szent Imre Teaching Hospital, Department of Angiology and Nephrology, Budapest, Hungary

The aim of our study was to evaluate microvascular reactivity and arterial stiffness with non-invasive methods in patients with different cardiovascular risk factors. Following blood pressure measurement, skin microcirculation was studied with laser Doppler flowmetry (Periflux 5001). The effect of local heating (LH; 44°C, 1 min) and the postocclusive reactive hyperaemia (PORH; 220 mmHg, 3 min) were measured. Arterial stiffness was evaluated with the newly developed TensioClinic Arteriograf instrument which calculate the pulse wave velocity (PWV, m/s) and augmentation index (Aix, %). Healthy controls (CONT, n = 13), patients with essential hypertension (EH, n = 13), with essential hypertension and peripheral artery disease (EH+PAD, n = 22), and essential hypertension and 2-type diabetes mellitus (EH+DM, n=25) were measured. Pulse pressure (PP) was higher in EH+PAD ( $62.6\pm3.2$  mmHg, p < 0.05) and EH+DM (67.6 $\pm$ 3.3 mmHg, p < 0.001) groups compared with CONT (52.5±3.4 mmHg). Aix, PWV and the PORH were significantly different in healthy controls (-62.11%, 7.01 m/s, 393.77%, resp.) compared to the patient groups. These parameters were significantly different in the EH (-34.25%, 7.91 m/s, 292.77%), EH+PAD (0.34%, 9.16 m/s, 182.86%) and EH+DM groups (0.87%, 9.27 m/s, 192.84%). The reactive hyperaemia for LH was significantly lower in the EH (782 $\pm$ 106%), EH+PAD (651 $\pm$ 53%) and EH+DM  $(453\pm45\%)$  compared with the CONT (1049 $\pm133\%$ ). Significant correlation was found between the PORH and Aix (r = -0.54; p < 0.001) and PP and Aix (r = 0.42, p < 0.05). Using these non-invasive methods there is a growing possibility to diagnose endothelial dysfunction in patients with different cardiovascular diseases. Prospective studies are needed to evaluate the prognostic value and the utility in therapy follow-up of these methods.

#### P.052 BLOOD PRESSURE AND LARGE ARTERIAL ELASTIC PROPERTIES. BENEFIT OF BETAXOLOL IN HYPERTENSION

F.T. Ageev, Y.A.A. Orlova\*, B.D. Kulev, O.N. Baldina. *Cardiology Research Center, Moscow, Russia* 

Background and Aim: Large artery damage is a major contributory factor to cardiovascular morbidity and mortality of patients with hypertension. As shown ASCOT and other study, beta-blockers appear to be less effective than other drugs in improving outcome in hypertensive patients, and a potential explanation may be that beta-blockers are less effective in reducing arterial stiffness. However, the aim of this study was to prove otherwise while assessing the direct effect of cardioselective beta-adrenoblocker betaxolol (Lokren) on arterial distensibility in patients with mild, moderate and severe hypertension.

Materials and Methods: 50 hypertensive patients (mean age  $54.7\pm14.3$  years, 28 male, 32 female) received betaxolol in individual titrated doses  $10-40\,\text{mg}$  (mean dose  $14.7\pm6.8\,\text{mg}$ ) daily for 3 months. The examination comprised routine tests, ECG, blood glucose, total cholesterol, triglycerides. The assessment of arterial stiffness was done by way of measuring brachial-ankle pulse wave velocity (baPWV). Systemic arterial compliance was estimated through brachial Augmentation Index ( $Al_D$ ), Endothelial function was calculated based on flow-mediated dilatation (FMD) parameters.

**Results:** The treatment produced a significant reduction in systolic  $(-27.2 \, \text{mmHg})$  and diastolic BP  $(-12.3 \, \text{mmHg})$ . No fluctuation of Alpwas monitored which should be attributed to the pulse decrease from 74.3 to 60.6 beats/min (p < 0.001). Significant decrease of baPWV (by 8.1%) and increase of FMD (by 10.9%) was observed. There was an insignificant rise