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P7: TELOMERE LENGTH AND AORTIC VALVE CALCIFICATION

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used as culturing substrates, which restrict cell migration although enabling biochemical communication. All the established culture systems presented viable and proliferative cell populations over time. Interestingly, the tri-culture system presented protein synthesis values much higher than the co-cultures, mostly of collagen. On the immunofluorescence micrographs were observed the maintenance of cell type-specific proteins expression, even in the presence of another cell type. Quantification of Growth Factors (GFs) on conditioned media of the co- and tri-culture systems demonstrated a synergistic interplay between Vascular Endothelial GF (VEGF) and basic Fibroblast GF (Bfgf). The VEGF was mainly expressed by smooth muscle cells, which leads to increasing levels in the co- and tri-culture systems. A similar trend is observed for Bfgf, expectedly produced by the fibroblastic cells. By its side, the platelet derived GF levels remain unaltered among conditions. This study demonstrated the fundamental importance of the intercellular crosstalk between endothelial, smooth muscle and fibroblastic cells. It reinforces the potential of a tri-culture system in the development of tissue engineered blood vessel substitutes.

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P4

MECHANISM OF PROANGIOGENIC ACTIVITY OF MITOCORRECTIN ON ENDOTHELIAL CELLS IN VITRO

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Background: Investigations of different effective treatment modalities of infectious and inflammatory complications of stroke remain relevant. Normalization of vascularization, impaired due to hypoxia, is an important component of ischemic disease treating. The aim of our work was to study the mechanism of action of mitocorrectin on endothelial cells in vitro.

Methods: Active ingredient of mitocorrectin is a set of oligopeptides and amino acids isolated from cell mitochondria of the liver, brain and the pancreas (10:10:1) of pigs. As an experimental model was used endothelial cell line (PAEC), which was incubated at the standard conditions. Cytotoxic/proliferative effect on cultured cells was determined using cytofluorimetric analysis and MTT-test.

Results: Our studies have shown that mitocorrectin increased of endothelial cell by 25% and decreased apoptotic cells almost 2 times compared with the control. Cytofluorimetric analysis revealed an increase 1.8-fold in the population of proliferative cells pool under the influence of mitocorrectin. The most pronounced mitogenic and antiapoptotic effect of mitocorrectin on the endothelial cells was at concentrations of 0.1 – 1/ml. Thus, these doses may be the most therapeutically effective in restoring vascularization in post-stroke period. In addition, long-term cultivation of cells in the 2D-culture when exposed to mitocorrectin, more intensive formation of the capillary-like structures compared with controls, which may indicate vascular morphogenesis.

Conclusions: Thus, a study suggests that mitocorrectin shows a positive proangiogenic effect on endothelial cell line and this drug can be quite effective to restore vascularization, which is important in post-stroke period at ischemic complications.

P5

REGIONAL VARIATIONS IN THE MICROMECHANICAL AND BIOCHEMICAL PROPERTIES OF THE OVINE AORTA

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Background: It is important to understand regional variations in the mechanical and biochemical properties of the aorta to better predict and treat

diseases. Although previous studies have been explored regional differences in the structure and biomechanical properties of the aorta, little is known about how these properties vary across its entire length [1, 2].

Objectives: To map the micromechanical and biochemical properties of the ovine aorta from the aortic root to the celiac artery region.

Methods: Fresh ovine aortas (n = 3) were split into nine sections, separated by 2 cm intervals between the aortic root and the celiac artery region. For each section, three biopsies were cut out using a 5 mm biopsy punch (a total of 81 biopsies). An oscillatory nanoindentation method was used to determine the micromechanical properties of the tissue [3]. 16 indents were made per biopsy. The shear storage (G'), the shear loss modulus (G'') were determined [3]. Subsequently, the same samples were used to determine elastin, collagen and glycosaminoglycan (GAG) levels using established biochemical assays.

Results: Overall, there was a significant correlation between an increase in G' and collagen (P = 0.01) with distance from the aortic root whilst elastin (P = 0.05) and GAG (P = 0.05) levels were significantly decreased.

Conclusions: Our study is the first to comprehensively map the mechanical and biochemical properties across the entire aorta. There was a progressive increase in mechanical properties from the proximal to the distal region, along with an increase in collagen and a decrease in elastin content.

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P6

ARTERIAL STRUCTURE AND COAGULATION IN AGEING NAKED MOLE RATS

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Vascular stiffening and a prothrombotic state consistently increase with age. Naked mole rats (NMRs) among rodent species have a maximum lifespan exceeding 30 years. Arterial stiffness assessed by pulse wave velocity and arterial pressure have been shown not to increase with age in NMRs (Grimes et al. *AJP*). The objective of this work was to study the relation between functional and structural arterial changes and plasma thrombin generation changes in young (2-year-old) and adult (9-year-old) NMRs. Collagen and elastin contents, vascular smooth muscle cell density and intimal thickening have been analyzed in the thoracic aorta, whereas plasma thrombin generation was assessed by calibrated automated thrombography associated with dosage of coagulation factors and endothelial markers. Our results showed no difference in collagen, elastin and vascular smooth muscle cell (VSMC) content between 2 (n = 5) and 9-year-old (n = 5) NMRs. There was no elastin degradation nor intimal thickening in NMRs at 9-years-old compared to 2-years-old. We showed no increase in plasma thrombin generation up to 9 years of age and no change in coagulant fibrinogen and factor VIII both known to increase normally with age. The expression of Endothelial Protein C Receptor (EPCR) and Thrombomodulin were similar at both ages.

In conclusion, young and adult NMRs do not show structural changes of the vascular wall in accordance with the absence of arterial stiffening. The conservation of an intact structure of the vascular wall and no change in endothelial markers during the first third of lifetime is compatible with the lack of a prothrombotic state.

P7

TELOMERE LENGTH AND AORTIC VALVE CALCIFICATION

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Background: Short telomere length (TL) is associated with atherosclerosis development. Aortic valve stenosis, an age-related disease characterized by narrowing of the aortic opening, is mainly caused by aortic valve

calcification. Development of aortic calcifications shares many similarities with atherogenesis, we thus hypothesize that people with short TL may have higher risk to develop aortic valve stenosis.

Methods: Aortic valves were obtained from 11 patients undergoing valve replacement surgery. Each valve cusp was macroscopically dissected into healthy, intermediate and calcified regions. DNA was extracted by phenol/chloroform method and TL measured by Southern blots of the terminal restriction fragments.

Results: TL from healthy and intermediate valve regions were similar and then merged in a non-calcified group. In all subjects, TL of calcified regions were shorter than TL in non-calcified regions. The gap between TL of non-calcified and calcified regions was 0,53kb ($p < 0.007$).

Conclusion: Calcified aortic valve regions have shorter telomere length than non-calcified. Directionality of the relationship between telomere dynamics and aortic valve stenosis will be explored *in vitro*.

P8

THE EFFECT OF CAFFEINE ON MENTAL STRESS RELATED CARDIOVASCULAR RESPONSE

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Background: Caffeine, the most widely used pharmacologically active substance causes mental stimulation and a slight raising of blood pressure. The aim of our work was to evaluate the effect of caffeine on the cardiovascular system during rest and during mental stress.

Methods: RR interval duration, arterial blood pressure and Laser-Doppler (LD) flux were monitored in 40 healthy volunteers (aged 21.98 ± 0.9 years) before and after ingestion of 200 mg of caffeine. The measurements were performed during rest (360s), during mental stress (90s) and during relaxation after mental stress (510s). The measurements were performed twice: under the effect of caffeine and under the effect of placebo. The study was approved by the National Medical Ethics Committee; written informed consent was obtained from each subject.

Results: During resting condition RR interval (ms) increased ($910,49 \pm 130,5$ before and $958,96 \pm 130,66$ after) ($p < 0,05$), systolic blood pressure (mm Hg) increased ($119,35 \pm 14,3$ before and $127,54 \pm 15,9$ after) ($p < 0,05$), diastolic blood pressure (mm Hg) increased ($68,78 \pm 11,2$ and $76,20 \pm 11,6$) ($p < 0,05$), LD flux decreased ($150,05 \pm 96,4$ and $115,15 \pm 86,7$) ($p < 0,05$) and temperature decreased ($30,92 \pm 3,5$ and $29,71 \pm 3,5$) ($p < 0,05$) after ingestion of caffeine. During mental stress systolic and diastolic blood pressure increased significantly less, RR interval was nearly the same and LD flux after mental stress increased more and earlier after ingestion of caffeine.

Conclusion: Although caffeine raises blood pressure it has favourable effect on the cardiovascular system during and after mental stress.

Poster Session I – Clinical aspects

P10

COMBINATION OF FLOW-MEDIATED DILATION AND PULSE WAVE VELOCITY PROVIDES FURTHER CARDIOVASCULAR RISK STRATIFICATION IN PATIENTS WITH CORONARY ARTERY DISEASE: FLOW-MEDIATED DILATION JAPAN STUDY A (FMD-J A)

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Purpose/Background/Objective: The usefulness of vascular function tests for management of patients with coronary artery disease (CAD) has not been fully investigated.

Methods: We measured flow-mediated vasodilation (FMD) and brachial-ankle pulse wave velocity (baPWV) in 462 patients with CAD for assessment of the predictive value of FMD and baPWV for cardiovascular events in a prospective multicenter observational study. The first primary outcome was

coronary events, and the second primary outcome was a composite of coronary events, stroke, heart failure, and sudden death.

Results: A median follow-up period was 49.2 months. First primary outcome occurred in 56 patients and the second primary outcome occurred in 66 patients. FMD above the cutoff value of 7.1%, derived from receiver-operator curve analyses for the first and second primary outcomes, was significantly associated with lower risk of the first (hazard ratio [HR], 0.27; 95% confidence interval [CI], 0.06–0.74; $P = 0.008$) and second (HR, 0.32; 95% CI, 0.09–0.79; $P = 0.01$) primary outcomes. baPWV above the cutoff value of 1731 cm/s was significantly associated with higher risk of the first (HR, 1.86; 95% CI, 1.01–3.44; $P = 0.04$) and second (HR, 2.19; 95% CI, 1.23–3.90; $P = 0.008$) primary outcomes. Among the four groups stratified according to the combination of cutoff values of FMD and baPWV, stepwise increases in the calculated risk ratio for the first and second primary outcomes were observed.

Conclusions: Both FMD and baPWV were independent predictors of cardiovascular events in patients with CAD. The combination of FMD and baPWV provided further cardiovascular risk stratification.

P11

EFFECT OF AGING ON THE PRESSURE ASYMPTOTE AND TIME CONSTANT OF EXPONENTIAL DIASTOLIC AORTIC PRESSURE DECAY IN HUMANS

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There are few data regarding the effect of aging on pressure asymptote (Pasymp) and time constant (Tau) of exponential diastolic aortic pressure (AoP) decay in normal human heart. To investigate this issue, we analyzed high-fidelity AoP, measured by use of a catheter-tipped manometer in 71 normal subjects who underwent diagnostic cardiac catheterization but who were found to have normal coronary artery and LV function. Subjects who had hypertension, diabetes or renal disease were excluded. There were 49 men and 22 women, ranging in age from 20 to 80 years. We analyzed diastolic AoP sampled every 5 ms from the point of minimal dP/dt to the top of ECG-R waves of the next beat, and estimated Tau and Pasymp by the exponential best fitting with a variable Pasymp results. Systolic AoP were significantly increased with age, but mean and diastolic AoP remained unchanged. Pasymp was 58.5 ± 8.1 mmHg and Tau was 436 ± 105 msec. Pasymp show no significant age-related change, but strongly and positively correlated with systolic, diastolic and mean AoP ($R^2 = 0.39, 0.70$ and 0.66 , respectively). For Tau, it was weakly and positively related with both age and AoP (Age: $R^2 = 0.20$, AoP: $R^2 = 0.08-0.20$).

Conclusion: We documented Pasymp and Tau of the Windkessel with the beating heart in normal humans. Tau was associated with aging, whereas Pasymp, which increased with the level of AoP, did not vary with aging per se, at least until the ninth decade. These data may provide insight into the understanding of AoP physiology.

P12

VALIDATION OF SYNTHESIZED CENTRAL PRESSURE WAVEFORM IN PATIENTS WITH AN INFRARENAL AORTIC ANEURYSM BEFORE AND AFTER ENDOVASCULAR REPAIR

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Background: Abdominal aortic aneurysm (AAA) disease is mainly treated by endovascular aneurysm repair (EVAR), which shows short-term advantages in terms of lower morbidity and mortality compared to open repair. Long-term outcome seems to be inferior with regard to survival. This could partly be explained by a change in dynamics of the aortic wall, including aortic central pressure (CP) waveforms, induced by the endograft (Figure). Arterial stiffness is predictive of cardiovascular disease but has not been investigated in AAA-patients. We investigated if CP and Augmentation index (AIX) can be calculated correctly in AAA-patients.