8.6: ELECTRICAL CAROTID BARORECEPTOR ACTIVATION LOWERS RENAL ARTERY IMPEDANCE AND STIFFNESS IN AN ACUTE CANINE MODEL

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INCREASED ARTERIAL STIFFNESS IN PATIENTS WITH ALPHA 1

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**Method:** The *in vitro* study consists of detection and characterisation of inflammatory markers on activated endothelial cells by immunocytochemistry and anti-E-selectin antibody conjugated USPIO. The ex vivo stage involves characterisation of inflammatory markers on atherosclerotic plaques, and finally the *in vivo* stage consists of development of a rat model with focal lesions in carotid arteries to allow targeted molecular imaging by MRI.

**Results:** We have established an *in vitro* cellular model of endothelial inflammation induced with TNFα. We have confirmed the inflammation of endothelial cells with both immunocytochemistry and MRI. These preliminary results revealed a temporal expression of the inflammatory markers, such as, E-selectin and VCAM-1, and the expression of these markers was dose dependent on exposure to TNFα. Furthermore, we imaged rat carotid arteries *in vivo* by MRI.

**Conclusion:** We successfully developed an *in vitro* model to detect and characterise inflamed endothelial cells by immunocytochemistry and MRI. This will allow us to develop agents and protocols for imaging vascular inflammation in atherosclerosis in the future. We have also successfully imaged the carotid arteries in a live rat by MRI. This pilot study will form the basis for a translational study to provide clinicians with a novel tool for *in vivo* assessment of atherosclerosis.

**8.4 ARTERIAL COMPLIANCE AND CAROTID ATHEROSCLEROSIS IN APOLIPOPROTEIN A-I AMYLOIDOSIS (LEUT75PRO)**

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**Background:** Hereditary amyloidosis are late-onset autosomal dominant disorders characterized by amyloid deposit in various tissues. Among them, Apolipoprotein A-I amyloidosis (Leu75Pro) is a rare autosomal dominant condition in which renal, hepatic, and testicular involvement have been demonstrated. No data are available about vascular alterations in this condition. Aim of the study was to evaluate arterial stiffness assessed by pulse wave velocity (PWV) and carotid artery intima-media thickness (IMT), evaluated by ultrasound, in patients with Apolipoprotein A-I amyloidosis (APO AI). Patients: In 104 patients with APO AI (mean age 52 ± 16 years, 56 F) and in 104 subjects matched for age, sex, BMI, BP, and heart rate were observed. PWV was significantly higher in patients with APO AI than controls (11.5 ± 2.9 and 10.7 ± 2.3, p < 0.05), even after adjusting for cholesterol, creatinine, mean BP and heart rate measured during PWV assessment. In patients with APO AI the prevalence of increased arterial stiffness (defined as PWV > 12 m/sec) was significantly greater than in controls (31% vs 17%, p < 0.05). Mean common, bifurcation and common carotid artery IMT were comparable in the two groups (8.7 ± 0.21 vs 8.8 ± 0.17; 2.13 ± 0.41 vs 1.25 ± 0.38; 0.35 ± 0.33 vs 0.95 ± 0.28 respectively for APO AI vs controls, p = ns). Similar results were obtained for MeanMax IMT and TMax (1.02 ± 0.29 vs 1.03 ± 0.26 and 1.60 ± 0.69 vs 1.56 ± 0.58 p = ns). Conclusion: In patients with Apolipoprotein A-I amyloidosis (Leu75Pro) a significant increase in arterial stiffness is observed, on the contrary carotid artery IMT is comparable to that of matched control subjects. These results may add significant information to the clinical features of this rare genetic disorder.

**8.5 INCREASED ARTERIAL STIFFNESS IN PATIENTS WITH ALPHA 1 ANTITRYPSIN DEFICIENCY**

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**Results:** By defining no differences for age, sex, BMI, BP, heart rate rates, were observed. PWV was significantly higher in patients with APO AI than controls (11.5 ± 2.9 and 10.7 ± 2.3, p < 0.05), even after adjusting for cholesterol, creatinine, mean BP and heart rate measured during PWV assessment. In patients with APO AI the prevalence of increased arterial stiffness (defined as PWV > 12 m/sec) was significantly greater than in controls (31% vs 17%, p < 0.05). Mean common, bifurcation and common carotid artery IMT were comparable in the two groups (8.7 ± 0.21 vs 8.8 ± 0.17; 2.13 ± 0.41 vs 1.25 ± 0.38; 0.35 ± 0.33 vs 0.95 ± 0.28 respectively for APO AI vs controls, p = ns). Similar results were obtained for MeanMax IMT and TMax (1.02 ± 0.29 vs 1.03 ± 0.26 and 1.60 ± 0.69 vs 1.56 ± 0.58 p = ns). Conclusion: In patients with Apolipoprotein A-I amyloidosis (Leu75Pro) a significant increase in arterial stiffness is observed, on the contrary carotid artery IMT is comparable to that of matched control subjects. These results may add significant information to the clinical features of this rare genetic disorder.

**8.6 ELECTRICAL CAROTID BARORECEPTOR ACTIVATION LOWERS RENAL ARTERY IMPEDANCE AND STIFFNESS IN AN ACUTE CANINE MODEL**

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**Background:** The exact mechanism by which electrical carotid baroreceptor activation (CBA) lowers blood pressure in patients with hypertension has yet to be fully elucidated. Given the central role of the kidneys in blood pressure regulation, the aim of this study was to assess the impact of CBA on renal artery impedance and hemodynamics.

**Materials and Methods:** Renal artery pressure (P) and flow velocity (U) were measured using an intravascular pressure-velocity wire catheter (Volcano Corp.) in 6 anaesthetised dogs at baseline (BL) and during CBA intended to produce a moderate reduction in mean arterial pressure. Mean flow velocity (Umean), systolic (SBP), diastolic (DBP) and mean pressure (MAP) were derived. Local pulse wave velocity (PWV) was derived from the upstroke of the PU-loops, and wave intensity analysis and wave decomposition was applied to assess (the ratio of) the backward and forward pressure wave (Pb/Pf). Renal artery input impedance was measured.

**Results (Table) and discussion:** CBA lowered blood pressure and reduced Pb, leading to higher Pb/Pf. CBA lowered the impedance modulus at all frequencies (DC component by 9%; harmonics on average by 28%). PWV concomitantly decreased significantly.

**Conclusions:** In an acute canine model, CBA has a profound effect of decreasing renal artery impedance and stiffness, suggesting that the therapy modulates renal artery tone and may have renoprotective effects by reducing the pulsatile energy in the microcirculation.