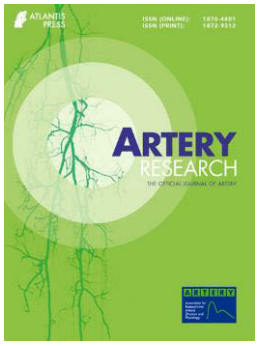

Artery Research

ISSN (Online): 1876-4401 **ISSN (Print): 1872-9312**
Journal Home Page: https://www.atlantis-press.com/journals/artres

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

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To cite this article: J.M. Duckers, D.J. Shale, N.S. Gale, R. Stockley, J.R. Cockcroft, C.E. Bolton (2009) 8.5: INCREASED ARTERIAL STIFFNESS IN PATIENTS WITH ALPHA 1 ANTITRYPSIN DEFICIENCY, Artery Research 3:4, 160–160, DOI: https://doi.org/10.1016/j.artres.2009.10.177

To link to this article: https://doi.org/10.1016/j.artres.2009.10.177

Published online: 14 December 2019

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Introduction: There is currently no clinical imaging techniques available to assess the degree of inflammation associated with atherosclerotic plaques. This study aims at visualising and characterising atherosclerosis using targeted USPIO as an MRI probe for detecting inflamed endothelial cells.
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 *in vivo* 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 (LEU75PRO)

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Background: Hereditary amyloidosis are late-onset autosomal dominant disorders characterized by amyloid deposition in various tissues. Among them, Apolipoprotein A-I amyloidosis (Leu75Pro) is a rare autosomal dominant condition in which renal, hepatic, and testicular involvement has 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 $\pm$ 16 years,56 F) and in 104 subjects matched for age, sex, body mass index (BMI) and blood pressure (BP), PWV and IMT were measured. **Results:** By definition no differences for age, sex, BMI, BP, heart rate were observed. PWV was significantly higher in patients with APO AI than controls (11.5 $\pm$ 2.9 and 10.7 $\pm$ 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 internal carotid artery IMT were comparable in the two groups(0.87 $\pm$ 0.21 vs 0.88 $\pm$ 0.17;1.23 $\pm$ 0.41 vs 1.25 $\pm$ 0.38;0.95 $\pm$ 0.33 vs 0.95 $\pm$ 0.28 respectively for APO AI vs controls,p=ns). Similar results were obtained for MeanMax IMT and TMax (1.02 $\pm$ 0.29 vs 1.03 $\pm$ 0.26 and 1.60 $\pm$ 0.69 vs 1.56 $\pm$ 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

J. M. Duckers [1], D. J. Shale [1], N. S. Gale [1], R. Stockley [2], J. R. Cockcroft [1], C. E. Bolton [1]
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Rationale: Alpha 1 Antitrypsin (AAT) deficiency is a familial cause of emphysema, due to reduced antiproteolytic activity within lungs. Systemic manifestations however, remain little explored. We have previously demonstrated increased arterial stiffness (AS) in patients with COPD and hypothesised that AAT deficient patients would present similarly but with lesser smoking exposure.
Methods: 19 AAT deficient patients, and 20 age, sex and smoking matched controls, all free of known cardiovascular disease were studied at clinical stability. All underwent spirometry (FEV_1), large artery haemodynamics including aortic pulse wave velocity (PWV), DEXA (body composition) and blood sampling (IL-6 & lipids).
Results: Age, heart rate, lipids and MAP were similar. Aortic PWV was greater in patients, than controls. Significant independent variables of aortic PWV in all subjects were age, FEV_1% and MAP, all $p < 0.001$. BMI and Fat free mass index (skeletal muscle mass) were lower in patients than controls, $p < 0.001$.
Conclusions: AAT deficient patients have increased AS, as determined by aortic PWV, which supports they are at increased cardiovascular risk.

Mean (SD)	Control (n = 20)	Patient (n = 19)
Men n (%)	13 (65)	12 (63)
Age (yrs)	61.1 (9.1)	59.2(12.1)
Smoke Pack yrs §	5.5 (0-70)	10.0 (0-60)
FEV_1 (% predicted)	100.8 (12.5)	42.7 (23.3)**
Heart rate (bpm)	68.2 (12.4)	75.7 (12.5)
MAP (mmHg)	100.4 (10.2)	101.5 (9.2)
Aortic PWV (m/s)	8.5 (1.6)	9.9 (2.1)*
AIx (%)	23.7 (8.8)	26.1 (6.5)
IL-6 (pg/ml) †	2.18 (1.64)	3.24 (1.62)*

* $p < 0.05$; ** $p < 0.001$. § median (range). † geometric mean (SD)

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 anaesthetized 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 derived.
Results (Table) and discussion: CBA lowered blood pressure and reduced Pf, 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.

	SBP mmHg	DBP mmHg	MAP mmHg	Umean cm/s	PWV m/s	Pf mmHg	Pb mmHg	Pb/Pf
BL	107.5(11.0)	69.8(15.8)	85.6(14.3)	29.5(5.4)	8.2(2.9)	34.7(6.0)	12.6(2.8)	0.37(0.08)
CBA	89.1(18.9)*	55.4(21.8)*	68.6(21.8)*	27.4(7.7)	5.4(1.7)*	29.3(3.6)*	12.7(2.5)	0.43(0.06)*

mean(standard deviation); *$P < 0.05$; paired T-test