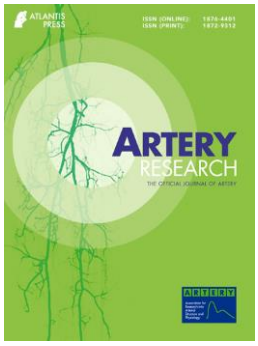


Artery Research

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

8.3: MRI OF ENDOTHELIAL ADHESION MOLECULES IN CAROTID ATHEROSCLEROSIS USING TARGETED ULTRASMALLSUPERPARAMAGNETIC PARTICLES OF IRON OXIDE (USPIO) - TOWARDS AN IN VIVO MODEL

J.M.S. Chan, K. Bhakoo, C. Monaco, R.G.J. Gibbs

To cite this article: J.M.S. Chan, K. Bhakoo, C. Monaco, R.G.J. Gibbs (2009) 8.3: MRI OF ENDOTHELIAL ADHESION MOLECULES IN CAROTID ATHEROSCLEROSIS USING TARGETED ULTRASMALLSUPERPARAMAGNETIC PARTICLES OF IRON OXIDE (USPIO) - TOWARDS AN IN VIVO MODEL, Artery Research 3:4, 159–160, DOI: https://doi.org/10.1016/j.artres.2009.10.175

To link to this article: https://doi.org/10.1016/j.artres.2009.10.175

Published online: 14 December 2019

Artery Research (2009) 3, 159–160

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/artres

Oral Presentation Abstracts

8.1
CENTRAL ARTERIAL STIFFNESS OCCURS IN BRONCHIECTASIS

N. S. Gale [1], J. M. Duckers [2], M. Munnery [3], S. Enright [1], J. R. Cockcroft [3], C. E. Bolton [2], D. J. Shale [2]

[1]*School of Healthcare Studies, Cardiff University, Cardiff, United Kingdom*
[2]*Department of Respiratory Medicine, Cardiff University, Cardiff, United Kingdom*
[3]*Wales Heart Research Institute, Cardiff University, Cardiff, United Kingdom*

Rationale: Bronchiectasis is characterised by inflammation and airways injury, which lead to loss of airways function, factors which are associated with an increased risk of cardiovascular disease (CVD) in various populations. Central arterial stiffness (AS) a predictor of CVD risk has not been studied in bronchiectasis. We hypothesised that patients with bronchiectasis would have increased AS.

Methods: We studied 20 clinically stable patients with bronchiectasis and 20 age, sex and smoking matched controls, without evidence of CVD. In all subjects we determined FEV_1, aortic pulse wave velocity (PWV), fasting lipids and systemic inflammation (IL-6).

Results: Aortic PWV and IL-6 were greater in patients, than controls ($p < 0.05$), while age, BMI, lipids and MAP were similar for patients and controls. In all subjects age was the only predictor of aortic PWV ($p < 0.01$).

Conclusions: Patients with bronchiectasis have increased AS, as determined by aortic PWV, which indicates an increased risk of CVD. Longer term studies are needed to determine the importance of this finding.

Mean (SD)	Control (n = 20)	Patient (n = 20)
Men n (%)	4 (20)	4 (20)
Age (yrs) §	62 (43-69)	65 (42-80)
Smoking Pack yrs §	0 (0-30)	0 (0-30)
FEV_1 (% predicted)	105.1 (9.1)	67.8 (25.8)**
Heart rate (bpm)	65.4 (9.4)	73.0 (11.9)*
MAP (mmHg)	100.1 (14.3)	103.2 (12.0)
Aortic PWV (m/s)	8.8 (1.6)	10.5 (3)*
AIx (%)	29.6 (8.8)	28.8 (8.7)
IL-6 (pg/ml) †	1.19 (3.7)	4.41 (5.81)*

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

8.2
COMPARISON OF THREE DIFFERENT METHODS TO CALCULATE AORTIC PULSE WAVE VELOCITY (PWV) USING A 1D MODEL OF THE SYSTEMIC CIRCULATION

B. Trachet [1], P. Reymond [2], J. Kips [1], A. Swillens [1], M. De Buyzere [3], B. Suys [4], N. Stergiopulos [2], P. Segers [1]

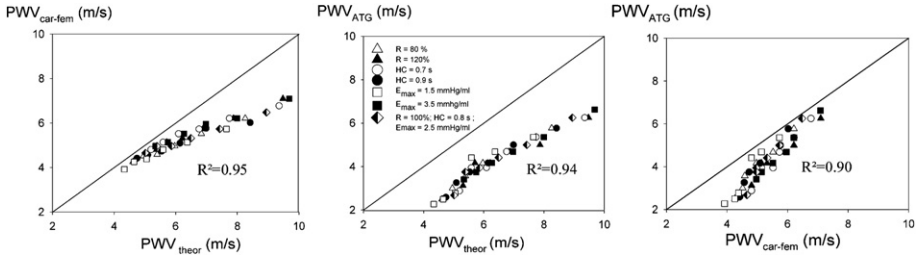
[1]*bioMMeda, Institute Biomedical Technology, Ghent University, Ghent, Belgium*
[2]*Laboratory of Hemodynamics and Cardiovascular Technology, Swiss Federal Institute of Technology, Lausanne, Switzerland*
[3]*Department of Cardiovascular Diseases, Ghent University Hospital, Ghent, Belgium*
[4]*Department of Pediatrics, Antwerp University, Belgium*

Aortic pulse wave velocity (PWV) is a measure of the stiffness of the large arteries, and is often used as indicator of clinical cardiovascular risk. Yet, methodological issues still exist on how PWV should best be measured. We have used a 1D arterial network computer model of the systemic circulation to compare three different methods to determine aortic PWV: $PWV_{car\text{-}fem}$ (~ carotid-femoral PWV, the current clinical gold standard method), PWV_{ATG} (~ PWV computed with a new device called Arteriograph, making use of only one brachial pressure recording) and PWV_{theor} (~ theoretical PWV according to the Bramwell-Hill equation). Different model parameters such as arterial distensibility, terminal resistance (R), cardiac contractility (Emax) and duration of the heart cycle (HC) were varied to obtain in total 42 different simulations. We found a good correlation between PWV_{theor} and $PWV_{car\text{-}fem}$ ($R^2 = 0.95$) or PWV_{ATG} ($R^2 = 0.94$) but the latter were systematically lower than PWV_{theor} (with 1.08 ± 0.70 m/s for $PWV_{car\text{-}fem}$ and 2.17 ± 0.42 m/s for PWV_{ATG} respectively). For both methods, Bland-Altman plots showed that the underestimation increases for higher values of PWV (figure not shown). Comparing $PWV_{car\text{-}fem}$ with PWV_{ATG}, both methods correlate well ($R^2 = 0.90$), with PWVcar-fem being on average 1.09 ± 0.48 m/s higher than PWV_{ATG}. In conclusion, in our computer model study, both the carotid-femoral PWV and the Arteriograph method provide values that correlate well to aortic PWV, but the actual values are lower than the theoretical ones following from the Bramwell-Hill formula.

8.3
MRI OF ENDOTHELIAL ADHESION MOLECULES IN CAROTID ATHEROSCLEROSIS USING TARGETED ULTRASMALL SUPERPARAMAGNETIC PARTICLES OF IRON OXIDE (USPIO) - TOWARDS AN IN VIVO MODEL

J. M. S. Chan [1], K. Bhakoo [2], C. Monaco [3], R. G. J. Gibbs [1]

[1]*Vascular Surgery Unit, St Mary's Hospital, Imperial College London, United Kingdom*



1872-9312/$ – see front matter

[2]*Stem Cell Imaging Group, Imperial College London, United Kingdom*
[3]*Kennedy Institute of Rheumatology, Imperial College London, United Kingdom*

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)

A. Paini [1], M. L. Muiesan [1], M. Salvetti [1], C. Aggiusti [1], E. Belotti [1], C. Agabiti Rosei [1], G. Gregorini [2], G. Cancarini [2], E. Agabiti Rosei [1]
[1]*Internal Medicine, University of Brescia, Brescia, Italy*
[2]*Nephrology, University of Brescia, Brescia, Italy*

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]
[1]*Cardiff University, Cardiff, United Kingdom*
[2]*University Hospitals Birmingham, Birmingham, United Kingdom*

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

P. Segers [1], D. Wagner [2], K. Ludwig [2], A. W. Cates [2], D. Georgakopoulos [2]
[1]*Ghent University, Gent, Belgium*
[2]*CVRx, Minneapolis, MN, USA*

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