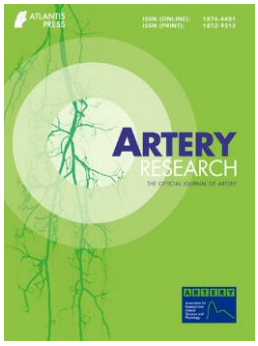

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P8.01: ENDOTHELIAL DYSFUNCTION AND LOW-GRADE INFLAMMATION ARE ASSOCIATED WITH ARTERIAL STIFFNESS IN HEALTHY ADULTS OVER A 6-YEAR PERIOD THE AMSTERDAM GROWTH AND HEALTH LONGITUDINAL STUDY (AGAHLS)

B.C.T. van Bussel, F. Schouten, R.M.A. Henry, C.G. Schalkwijk, M.R. de Boer, I. Ferreira, Y.M. Smulders, J.W.R. Twisk, C.D.A. Stehouwer

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Background: The assessment of arterial stiffness and central pressures has been limited to specialised techniques and settings. New, more practical methods (ARCSolver) allow assessment using a standard brachial cuff. The objective was to assess the feasibility of central haemodynamics and surrogates of arterial stiffness from the ARCSolver in a community based setting.
Methods: Peripheral and central systolic and diastolic blood pressure (BP) and wave reflection parameters (augmentation index) were obtained from a 1,903 volunteers in an Austrian community setting. We assessed for known differences and associations according to gender and each age deciles from $<$30 years to $\geq$80 years in the whole population and a subset with a systolic BP $<$ 140 mmHg.
Results: Age and gender associations with central haemodynamic and augmentation parameters reflected those previously established from gold-standard non-invasive techniques under specialised settings (Fig. 1). Findings were the same for patients with a systolic BP below 140 mmHg (i.e. normotensive). Differences in actual values for augmentation index are likely due to lower numbers of volunteers in these age groups and method differences.
Conclusion: One-off measures of central haemodynamics and pulse wave augmentation from the ARCSolver demonstrated known age and gender associations which were not limited to normotensive individuals. Using ARCSolver to obtain estimates of central pressure and augmentation appears robust and feasible in a community setting. Further validation is now possible in large cohort studies, particularly in primary care settings.

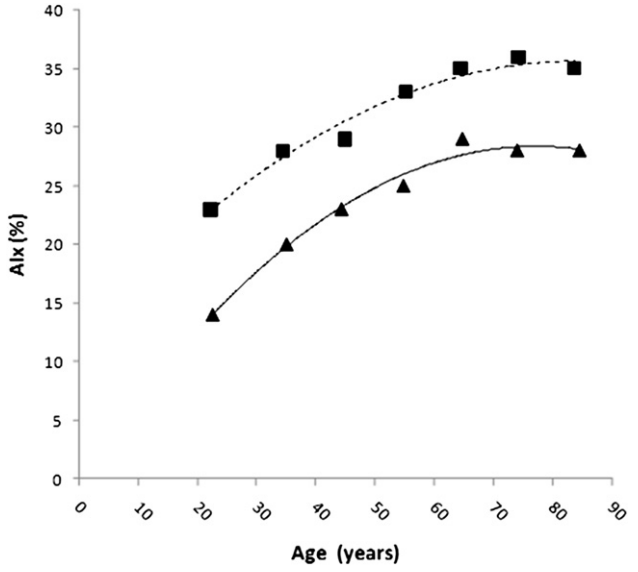

Figure 1 Regression curves for the effect of age on augmentation index in males (▲) and females (■)

P8 — Endothelium and Small Arteries 2

P8.01
ENDOTHELIAL DYSFUNCTION AND LOW-GRADE INFLAMMATION ARE ASSOCIATED WITH ARTERIAL STIFFNESS IN HEALTHY ADULTS OVER A 6-YEAR PERIOD
THE AMSTERDAM GROWTH AND HEALTH LONGITUDINAL STUDY (AGAHLS)

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Endothelial dysfunction and low-grade inflammation are associated with cardiovascular disease. Arterial stiffening plays an important role in cardiovascular disease and thus may be a mechanism through which endothelial dysfunction and/or low-grade inflammation lead to cardiovascular disease. We investigated the associations between, on the one hand, biomarkers of endothelial dysfunction (soluble endothelial selectin, thrombomodulin and both vascular- and intercellular adhesion molecules 1 and von Willebrand factor) and of low-grade inflammation (C-reactive protein, serum amyloïd A, interleukin 6, interleukin 8, tumour necrosis factor α and soluble intercellular adhesion molecule 1) and, on the other hand, arterial stiffness over a 6-year period, in 293 healthy adults (155 women). Biomarkers were combined into mean Z-scores. Carotid, femoral and brachial arterial stiffness and carotid-femoral pulse wave velocity were determined by ultrasonography. Measurements were obtained when individuals were 36 and 42 years of age. Associations were analysed with generalised estimating equation and adjusted for sex, height and mean arterial pressure. The endothelial dysfunction Z-score was inversely associated with femoral distensibility [β(95%CI)-0.51(-0.95;-0.06)] and compliance coefficients [-0.041(-0.076;-0.006)], but not with carotid or brachial stiffness or carotid-femoral pulse wave velocity. The low-grade inflammation Z-score was inversely associated with femoral distensibility [-0.51(-0.95;-0.07)] and compliance coefficients [-0.050(-0.084;-0.016)], and with carotid distensibility coefficient [-0.91(-1.81;-0.008)], but not with brachial stiffness or carotid-femoral pulse wave velocity. Biomarkers of endothelial dysfunction and low-grade inflammation are associated with greater arterial stiffness. This provides evidence that arterial stiffening may be a mechanism through which endothelial dysfunction and low-grade inflammation lead to cardiovascular disease.

P8.02
CHARACTERIZATION OF THE VASORELAXANT MECHANISMS OF ENDOCANNABINOID OLEOYLETHANOLAMIDE IN THE BOVINE OPHTHALMIC ARTERY

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Background: *Numerous studies show the potential therapeutic effect of different endocannabinoids and in particular the vasorelaxant effects in several vascular beds*

***Aim*:** To evaluate the vasorelaxant effect of oleoylethanolamide on isolated bovine ophthalmic arteries and to evaluate the possible mechanisms involved in relaxant responses.
***Methods*:** Ophthalmic arteries were isolated from bovine eyes and mounted in a wire miograph for isometric tension recording. The effects time- and concentration-dependent were assayed by addition of the oleoylethanolamide to the organ bath.
***Results*:** Oleoylethanolamide (0.1 - 10 μM) produced a significant concentration- and time-dependent vasorelaxation in the bovine ophthalmic artery pre-contracted with 5-HT (1 μM). The removal of endothelium provoked a slight reduction of the relaxant effects. Interestingly, a pre-treatment with antagonist PPARα GW6471 (1 μM) inhibited the concentration- and time-dependent oleoylethanolamide-induced vasorelaxation.
***Conclusion*:** The present study shows that oleoylethanolamide relaxed the isolated bovine ophthalmic artery in the concentration- and time-dependent manner. The candidate responsible of the vasorelaxant response to oleoylethanolamide appear to be the PPARα. This relaxant effect is an exciting tool to prevent ischemic injury because it improves the blood supply to the retina.

P8.04
DIFFERENT EFFECTS OF PLASMA MEMBRANE CALCIUM ATPASE 4 (PMCA4) ABLATION AND ACUTE INHIBITION ON CONTRACTILITY OF ISOLATED MOUSE MESENTERIC ARTERIES

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Plasma Membrane Calcium ATPases (PMCAs') are calcium extrusion pumps which may also modulate signal transduction. The most abundant PMCA