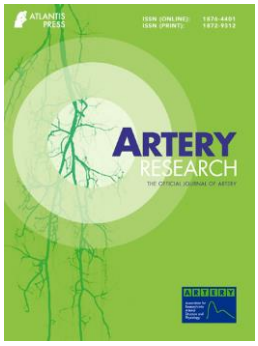

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P4.10: THE SEMICARBAZIDE-SENSITIVE AMINE OXIDASE (SSAO): A NEW ACTOR IN ATHEROSCLEROSIS IN THE APOE MOUSE MODEL?

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P4.10
THE SEMICARBAZIDE-SENSITIVE AMINE OXIDASE (SSAO): A NEW ACTOR IN ATHEROSCLEROSIS IN THE APOE MOUSE MODEL?

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The expression of « semicarbazide sensitive amine oxidase » (SSAO), an enzyme which transforms primary amines into aldehydes, ammonia and hydrogen peroxide, increases during smooth muscle cell differentiation (VSMC) and is widely expressed in the media layer from the arterial wall. The SSAO has been implicated in LDL oxidation and in inflammation. We hypothesized that the absence of SSAO should prevent the development of atherosclerosis. The progression of the disease and the implicated mechanisms were studied in double ApoE/SSAO knock out mice (ApoE-/-SSAO-/-) established in the laboratory.
Surprisingly 25 week-old ApoE-/-SSAO-/- mice presented a significant 50 % increase in plaque surface associated with an 80% decrease in a-actin expression in the media of aortic sinus from ApoE-/-SSAO-/- mice compared to ApoE-/- mice. We noticed a small T-cell infiltration in the media from ApoE-/-SSAO-/- mice whereas no T-cell infiltration was observed in the media from ApoE-/- mice. No difference was detected in monocytes/macrophages infiltration in the plaque in aortic sinus from APOE-/-SSAO-/- mice and ApoE-/-. The pro- (TNFa and INFg) and anti-inflammatory (IL10 and TGFb) cytokine expressions were similar in the spleen from ApoE-/- and ApoE-/-SSAO-/- measured at 25 and 15 week old.
In conclusion, the absence of the SSAO increases the atherosclerosis in ApoE-/- mice. This result could be explained either by a modification of VSMC phenotype or to an increase in VSMC apoptosis in inflammatory situation. Thus, the SSAO could be a new potential actor implicated in the inhibition of atherosclerosis development.

P4.11
GALECTIN-3 IS A POTENTIAL MEDIATOR OF ALDOSTERONE EFFECTS IN VASCULAR REMODELING

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Background. Aldosterone (Aldo) plays a major role in extracellular matrix (ECM) remodeling leading to heart failure (HF), but the mechanisms remained unclear. Galectin-3 (Gal-3), a β-galactosidase-binding lectin, plays an important role in inflammation and HF. We investigated whether Gal-3 mediates Aldo-induced ECM remodeling in vascular smooth muscle cells (VSMCs) *in vitro* and *in vivo*.
Methods. *In vitro*, primary cultured VSMCs were stimulated with Aldo (10^{-8}M) for 24h, with or without mineralocorticoid receptor (MR) antagonist. Gal-3 was over-expressed (transfection) and knocked-down (siRNA). Gal-3 expression and ECM production were evaluated by RT-PCR, Western blot and immunohistochemistry. *In vivo*, Wistar rats were treated by Aldo (1mg/kg/day)+salt or Aldo+salt+spironolactone (200mg/kg/day) for 3 weeks. Gal-3 and ECM proteins (collagen type I and III, fibronectin and elastin) were quantified by Western Blot and immunohistochemistry, and metalloproteinase (MMP) activities by zymography.
Results. *In vitro*, VSMCs spontaneously expressed Gal-3. Gal-3 over-expression enhanced ECM synthesis. Aldo up-regulated Gal-3 and ECM protein expression via MR. The Gal-3 silencing blocked Aldo-induced ECM production by VSMCs. In Aldo-salt hypertensive rats, Gal-3 aortic expression, ECM proteins and MMP activities were enhanced. Spironolactone treatment reversed all the above effects. Aortic Gal-3 expression was positively correlated with collagen type I, elastin, MMP-2 and MMP-13 activity.
Conclusions. Gal-3 is spontaneously expressed by VSMCs and induces ECM synthesis. It mediates Aldo-induced ECM remodeling via MR activation *in vitro* and *in vivo*. Our data suggest a key role for Gal-3 in Aldo-induced vascular alterations.

P4.12
MODEL BASED ESTIMATION OF AORTIC PULSE WAVE VELOCITY

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The proposed model is inspired by the theoretical frameworks of (1) Moens-Korteweg, (2) Bramwell & Hill, (3) Waterhammer equation used in ARCSolver. All of the mentioned equations allow the determination of velocity in an elastic tube from a single point measurement. Whereby Moens-Korteweg consider the tension of the wall and the radius of the vessel as well as the viscosity of blood which can be assumed constant and near one in the human circulation for simplicity. It's now not really surprising that with increasing pressure both wall tension and wall radius will elevate. In younger age both parameters likely to the same extent and with only minor effects on PWV. With increasing age distensibility of the arterial wall degenerates. Subsequently an increase in pressure will not be compensated by a diameter change, even more tension within the wall will increase and PWV as well. All changes affect PWV non linear. Equation 2 rewrites equation 1 to consider observable variables like pressure and volume flow. Simply spoken, PWV is a result of pressure changes and volume displacement. In complex transmission line theory using Fourier analysis, the relation between arterial flow and blood pressure is described by the so called characteristic impedance (Zc) illustrated in the Waterhammer Equation (3). ARCSolver calculates (Zc) using an adopted Windkessel model. Determinants of ARCSolver-PWV are wall tension (impedance), aortic blood pressure and age.

P4.13
RELATION OF AORTIC AUGMENTATION INDEX TO ARTERIAL AND VENTRICULAR PROPERTIES

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Aortic augmentation index, the amount by which aortic pressure is "augmented" above the first systolic shoulder of the aortic pulse wave, expressed as a ratio of aortic pulse pressure, is thought to relate to arterial properties. In particular it has been cited as an index of "arterial wave reflection" related to arterial stiffness. However, it could also be influenced by the characteristics of ventricular ejection. The objective of the present study was to examine the relation of AIx to arterial stiffness and ventricular contraction-relaxation. We studied 74 asymptomatic subjects, aged 24-89 years, 7-15 subjects per decade) using an Aloka α10 ultrasound system with 3MHz cardiac probe to perform conventional echocardiography, obtain tissue Doppler ventricular velocities and mitral flow velocities. Using the same system with a 10MHz linear vascular transducer, ECG-referenced echo-tracking of the carotid and femoral arteries was used to obtain carotid augmentation index (AIx) and carotid-femoral pulse wave velocity (PWV). The relation of AIx to PWV and ventricular tissue velocities was examined using univariable and multivariable regression analysis. On multivariable analysis, entering age, mean arterial blood pressure and all measures correlated with AIx on univariable analysis (including PWV), AIx was independently negatively correlated only with heart rate and the ratio of diastolic to atrial mitral valve flow velocities (E/A). Together these variables explained 39% of the variability in AIx. These results suggest that AIx is more closely related to ventricular contraction-relaxation than to arterial properties.

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P5.01
PRE-PREGNANCY TO EARLY PREGNANCY CHANGES IN MATERNAL CARDIOVASCULAR PHYSIOLOGY

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Maternal heart rate, blood pressure and cardiac output change as early as 5-6weeks in pregnancy. However, most of the longitudinal studies assessing maternal haemodynamic adaptation have used late first trimester