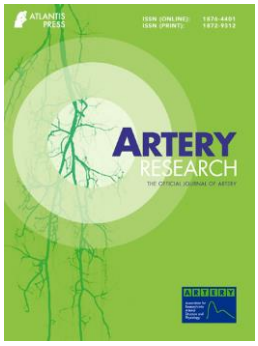

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P7.04: EVALUATION OF AORTIC STIFFENING IN HYPERTENSIVE RAT MODELS IN VIVO VIA ECHOTRACKING: PULSATILE DISTENSION WAVEFORM ANALYSIS

C. Vayssettes-Courchay, C. Ragonnet, M. Isabelle, T.J. Verbeuren

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Results: The results are shown in the table:

Variable	CTRL	P-value	OVX	P-value	OVX+Ω3
Final body weight (gr)	211±3,85	0,005	246,4±11,7	< 0,0001vsCTRL	263,3±7,3
c-fPWV cm/sec	378,9±7,2	<,0001	560,8±12,1	< 0,0001	363,3±5,9
MeanBP mmHg	108,8±4,8	0,002	129,8±2,6	0,003	109,3±2,7
Superoxide nmol/min/mm^2	97,4±8,3	0,01	142,3±14,6	0,04	105,0±9,8
SystolicBP mmHg	133,1±6,1	0,07	153,3±12,9	0,11	135,9±4,1
DiastolicBP mmHg	96,7±4,6	0,09	109,1±6,9	0,1	97,2±2,6
Ω3 index, percent	3,2±0,1	0,01	2,5±0,08	< 0,0001< 0,0001vsCTRL	5,2±0,2

Conclusions: Ω3 supplementation reduces arterial BP and restores mechanical arterial properties in a post menopause experimental model, likely by restoring NO availability.

P7.02
EFFECT OF CAPTOPRIL AND TELMISARTAN ON ANTI-CONTRACTILE PROPERTY OF PERIVASCULAR ADIPOSE TISSUE LOST AFTER HYPOXIA IN RAT MESENTERIC SMALL RESISTANCE ARTERIES

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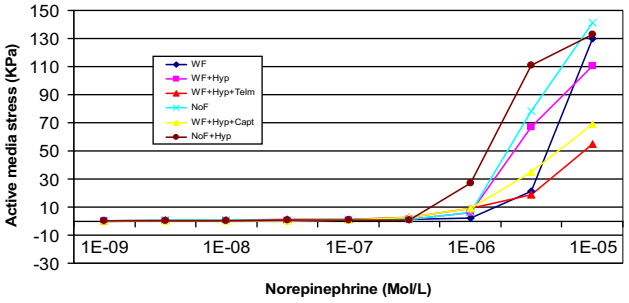
It has been previously demonstrated that inflammation in adipose tissue may be implicated in vascular dysfunction. Adipocytes secrete adiponectin, a physiological modulator of local vascular tone through an increased nitric oxide bioavailability. This capacity is lost in obesity by the development of adipocyte hypertrophy, leading to hypoxia, inflammation, and oxidative stress.
Aim: of the study was to investigate the feasibility a pharmacological modulation of the concerned effect, during hypoxia, in Wistar-Kyoto normotensive rats(WKY).
Materials and Methods: we investigated 25 WKY of 12 weeks of age. Mesenteric small resistance arteries were dissected and mounted on a wire myograph, according to Mulvany-Halpern technique(internal diameter about 200 μm). A concentration-response to norepinephrine(NE, from 10^{-9}to10^{-5}Mol/l)was evaluated in the following conditions:1)in vessels with perivascular fat tissue(WF),2)in vessels without perivascular fat tissue(NoF);3)in WF vessels under hypoxic condition(WF+Hyp);4)in NoF vessels under hypoxic condition(NoF+Hyp);5)in WF+Hyp vessels incubated with telmisartan10^{-2}Mol/l (WF+Hyp+Telm)or captopril10^{-2}Mol/l for 3hour(WF+Hyp+Capt).
Results: Are summarized in the figure(active media stress: KPa, mean of two vessels for each rat). A significantly greater reactivity to NE was observed in NoF vessels compared with WF vessels(ANOVAp=0.003between curves). This increased reactivity is similar to that observed in WF+Hyp(ANOVAp= NS between, NoF and WF+Hyp). Captopril and Telmisartan were able to prevent the effect of hypoxia(ANOVA $p<0.05$ between WF+Hyp and WF+Hyp+Capt or Telm).
In conclusion the ACE inihibitor captopril and the angiotensin-receptor blocker telmisartan seem to be able to restore the anti-contractile effects of perivascular fat tissue lost after hypoxia, possibly through an inihibition of angiotensin II effects.



P7.03
DIFFERENT EFFECT OF NEURONAL AND ENDOTHELIAL NOS INHIBITION ON HEART, CORONARY AND CAROTID ARTERY OF WISTAR RATS

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Long-term decrease of nitric oxide (NO) production evokes alterations in function and structure of cardiovascular system. We demonstrate the long-term effect of NO synthases inhibition with two different inhibitors on blood pressure (BP), heart and structure of coronary and carotid arteries. Four groups of ten weeks old Wistar rats were used: 1) control rats and rats receiving 2) N^G-nitro-L-arginine methylester (L-NAME) (50 mg/kg/day in tap water), 3) 7-nitroindazole (7NI) (10 mg/kg/day in tap water), 4) the same doses of L-NAME (in tap water) and 7NI (in pellet diet). The experiment lasted 6 weeks. BP was measured by the plethysmographic method weekly. At the end of the experiment the animals were perfusion with a glutaraldehyde fixative (120 mmHg) and heart, coronary and carotid artery were excised and processed for electron microscopy.

	Wistar	L-NAME	7NI	L-NAME+7NI
BP (mmHg)	112±2.20	164±2.10*	118±1,90^{+}	131±5,12$^{*+\#}$
H/B (mg/g)	3,08±0,14	3,41±0,13*	2,64±0,10^{*+}	3,07±0,12$^{+\#}$
Coronary a. CSA (μm^2)	8860±800	18280±1320*	6780±610^{*+}	14250±2290 $^{*+\#}$
Carotid a. CSA (μm^2)	69190±2460	109780±4040*	54290±2200^{*+}	88950±4340$^{*+\#}$

Blood pressure (BP), heart/body weight (H/B), cross sectional area — intima +media (CSA). *P<0.01 vs. Wistar, $^{+}$P<0.01 vs. L-NAME, $^{\#}$P<0.01 vs. 7NI
The study revealed, for the first time, that long-term inhibition of nNOS with 7NI, contrary to eNOS inhibition with nonspecific inhibitor L-NAME, evoked pressure independent cardiac hypotrophy and hypotrophy of the vessel wall. The data suggested that long-term nNOS inhibition likely iniciates a different chain of events leading to alterations in cardiovacular system then those after eNOS inhibition.
The study was supported by VEGA grant 2/0111/10, 2/0019/09.

P7.04
EVALUATION OF AORTIC STIFFENING IN HYPERTENSIVE RAT MODELS IN VIVO VIA ECHOTRACKING: PULSATILE DISTENSION WAVEFORM ANALYSIS

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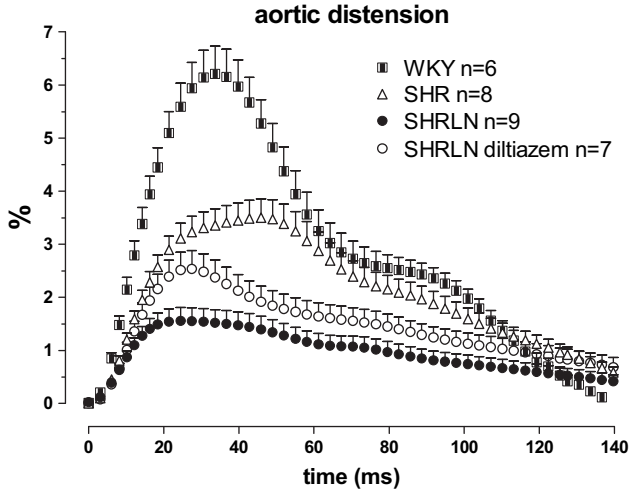
Objectives: Large artery stiffening, a risk factor in cardiovascular diseases, can be evaluated in human and rats by pulse wave velocity and echotracking, but controversies remain regarding the roles of blood pressure (BP) and vascular wall properties. We studied these points with the echotracking device ArtLab in the hypertensive rat (SHR) treated with L-NAME (SHRLN) to reduce nitric oxide levels.
Methods: In anaesthetized normotensive rats (WKY), SHR and SHRLN 20 weeks old, aortic BP is recorded via a catheter and diameter via the ArtLab ultrasound probe, in a motion mode to detect pulsatile displacement of aortic walls (distension). Data are analysed via a Matlab software.
Results: Compliance and distensibility are decreased in SHRLN (<SHR<WKY) and stiffness index increased. From distension-pressure loop curves, ascending, descending slopes and isobaric ascending slope at 200 mmHg are reduced in SHRLN<SHR<WKY. If we plot pulsatile time-waveform curves of pulse pressure (PP) and distension in % (Figure), maximal values and waves kinetics are altered. We therefore calculate a distensibility index as area under the curves of distension/PP. Diltiazem i.v. in SHRLN decreases systolic BP and PP to values similar to those in WKY; compliance, distensibility and stiffness reach only the values of SHR. Isobaric compliance at 160 mmHg is < than in WKY and distension remains lower than in SHR.
Conclusions: This study shows that 1) the ArtLab device analyses accurately compliance and stiffness indexes in animal models and 2) adding an analysis of aortic distension pulse waveform allows additional evaluation of BP-independent vascular wall stiffening.



P7.05
AORTIC STENT IMPLANTATION IN THE ISTHMIC REGION IN AN ANIMAL MODEL

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Background: Balloon dilation with stent implantation is a novel technique of aortic coarctation treatment. Residual arterial hypertension is a frequent finding (50% of treated patients), leading to major cardiovascular events and reducing life expectancy, even in the presence of stenosis resolution,
Aim of This Study: To determine feasibility of stent implantation in the aortic isthmus of an ovine model for the study of pressor, haemodynamic and hormonal changes induced in the growing animal.
Materials and Methods: Platinum-iridium stent was implanted in the aortic isthmus of 6 females sheep through vascular catheterization (STENT group). Vascular catheterization and angiographic study was performed in 6 control sheep (SHAM). All subjects had direct aortic pressure measurement during catheterization as well as echocardiographic and blood pressure measurements (through auricular artery catheterization) every 90 days. Twelve months after intervention the animals were sacrificed.
Results: Stent implantation did not affect growth and quality of life of the animals. Aortic pressure measurements performed during catheterization revealed a pressure wave morphology compatible with acute *augmentation index* alteration after stenting implantation. Auricular blood pressure did not differ among groups. One subject died after surgery for vascular access haemorrhage. Another subject died a few days after intervention. One subject developed aortic insufficiency after catheterization.
Conclusions: Stent implantation is feasible and well tolerated. This animal model can be useful to study the hemodynamic impact and the aortic stiffness induced by stent implantation and their consequences on the left ventricle and the vasculature.

Methodology
P8.01
REFERENCE VALUES FOR CAROTID STIFFNESS AND IMT

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Arterial properties, such as carotid distention and intima-media thickness (IMT) are important markers of arterial stiffness and atherosclerotic disease and have been shown to predict cardiovascular events. However, the application of these measurements in clinical practice has been hampered by the absence of reference values. The aim of the present study is to establish reference and normal values for carotid stiffness and IMT.
Measurements of carotid wall thickness and function obtained by an echo tracking system (Walltrack and ArtLab, Esaote, Maastricht, Netherlands) are available for individuals from several combined European (n ~9000) and Chinese (n ~1500) cohort studies. After pooling, data will be analysed in order to obtain normal values of carotid stiffness and IMT as estimated in the 'normal population', which will be constituted from those selected individuals with no acquired cardiovascular risk factors (i.e. diabetes, use of antihypertensive and/or lipid lowering medication, dyslipidaemia, smoking) or overt cardiovascular disease *and* optimal blood pressure values. Other populations with one or more risk factors will serve to scale stiffness and IMT between populations and to obtain reference values. A special attention will be focused on bringing correspondence between echo tracking and image analysis techniques to allow for conversion, and carotid stiffness values calculated from central pressure and/or brachial pressure.
The study is currently ongoing, which enables presentation of the exact design. Definitive results are expected for Artery 2011.

P8.02
LARGE DIFFERENCES IN CENTRAL PRESSURE ESTIMATION BETWEEN SPHYGMOCOR AND OMRON HEM 9000AI

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Introduction: Central systolic blood pressure (cSBP) has been shown to have a higher predictive value than brachial (cuff) pressure. Accurate cSBP, however, is difficult to obtain non-invasively and is often estimated from carotid or transformed peripheral pressures. In this study, the cSBP estimate from the Omron HEM 9000AI was compared to the SphygmoCor cSBP estimate and to carotid SBP. Whilst SphygmoCor uses a radial-to-aortic transfer function to calculate cSBP, the Omron HEM 9000 AI uses a regression equation which relies on the correlation between the second systolic peak of the radial pressure waveform and cSBP.
Methods: Radial applanation tonometry was performed in 251 rural black South Africans (aged 36-91 years) enrolled in the PURE study. Each subject was measured with an Omron HEM 9000AI and a SphygmoCor. Four different estimates of central pressure were calculated: (i) Omron device (cSBP-Omron); (ii) SphygmoCor, with calibration of the radial pressure by brachial SBP and DBP (cSBP-Sphygmo); (iii) SphygmoCor, with calibration of the radial pressure by brachial MAP and DBP obtained from brachial tonometry (cSBP-Sphygmo2, N = 201) and (iv) carotid SBP obtained through carotid tonometry calibrated with brachial MAP and DBP (cSBP-carotid, N = 143).

	Mean (SD) [mmHg]
cSBP-Omron	145.9 (25.5)
cSBP-Sphymo	127.4 (22.5)
cSBP-Sphymo2	131.2 (24.4)
cSBP-Carotid	138.0 (26.4)