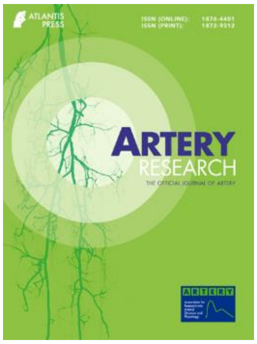

Artery Research

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

P8.13: A 1-D MODEL OF THE SYSTEMIC ARTERIAL TREE IN MICE

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To cite this article: L. Aslanidou, B. Trachet, P. Reymond, P. Segers, N. Stergiopulos (2014) P8.13: A 1-D MODEL OF THE SYSTEMIC ARTERIAL TREE IN MICE, Artery Research 8:4, 154–154, DOI: https://doi.org/10.1016/j.artres.2014.09.188

To link to this article: https://doi.org/10.1016/j.artres.2014.09.188

Published online: 7 December 2019

Madrid (UCM;GR-921641), Fundación Universitaria San Pablo-CEU, Fundación Mutua Madrileña and Sociedad para el Estudio de la Salud Cardiometabólica (SESCAMET).

P8.12
ARTERIAL DISTENSION-PRESSURE LOOP ANALYSIS IN HYPERTENSIVE RATS: ADVANTAGES, PITFALLS AND POSSIBILITIES

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Arterial wall viscosity (AWV) of central arteries, as well as distensibility, is important to properly buffer systolic ejection pressure. AWV is measured either by the area within the hysteresis of distension-pressure (DD-P) loop, defined as the viscous energy (AWV=Ve) or the ratio of Ve/Ve+energy stored during systole (=AWV%). We record DD-P loop via echotracking; averaged over 30 cardiac cycles, AWV and AWV% are calculated via MatLab software. Here we perform a post analysis of the DD-P loop in 12 groups of rats (n=5-8): normo- or hypertensive, with and without arterial remodeling, at different operating blood pressures (BP), using different compounds. AWV decreases and DD-P loop is flattened with increased BP; moreover it is differently altered if pulse pressure (PP) is altered and remains low at any operating BP in models with vascular wall remodeling. However in all conditions the ratio AWV% is poorly modified. Our results suggest that the AWV as the Ve (hysteresis loop area) is the most relevant in defining the viscous properties of the artery; they indicate that mean operating BP, PP and structural distensibility independently participate in modifying the shape of the loop which is largely dependent on the delay between peak systolic pressure and peak systolic diameter, apparent in the higher BP of the loop. This suggests that isobaric distensibility cannot be compared in the lower and upper part of the loop but only at a similar mean BP. Further studies will aim to confirm these suggestions and determine how to improve loop hysteresis evaluation

P8.13
A 1-D MODEL OF THE SYSTEMIC ARTERIAL TREE IN MICE

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Cardiovascular diseases are often studied at a pre-clinical stage using dedicated mouse models. However, (non-)invasive measurements in the murine cardiovascular system are difficult to obtain, limited to a restricted number of aortic locations, and need to be justified from an ethical perspective. In this work we present a 1-D model of the systemic circulation in mice. Murine arterial tree dimensions have been acquired and averaged from the segmentation of Micro-Computed Tomography (μ-CT) scans of 3 wild-type C57Bl/6 mice (12-15 weeks old). The resulting geometry consists of 85 arterial segments, including all major aortic branches as well as the tail and the cerebral tree. The remaining input to the model has been obtained from a wide range of literature data. An empirical relationship has been fitted to estimate the local arterial wall distensibility in all segments. Peripheral vessels are terminated with three-element windkessel models to account for the resistance and compliance of the distal vasculature. The integrated form of the momentum and continuity equations is solved numerically to yield pressures and flows throughout the arterial network. The model predicts pressure and velocity waveforms in good qualitative and semi-quantitative agreement with invasive pressure measurements as well as high-frequency ultrasound Pulsed-Wave Doppler aortic velocity and M-mode aortic distensibility measurements. In conclusion, a well-tuned and appropriately validated 1-D model for the murine cardiovascular system has been developed, which is ready to serve as a versatile study tool in the field of pre-clinical cardiovascular research.

P9.1
INFLUENCE OF INSULIN SENSITIVITY AND RELATED METABOLIC FEATURES ON CAROTID AND AORTIC STIFFNESS IN NORMAL SUBJECTS

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Insulin resistance (IR) underlies a cluster of metabolic abnormalities contributing to atherosclerosis. Relations between IR and large artery involvement in subjects without atherosclerotic disease are still debated.
Aim: to investigate in normal subjects the relations between IR and its associated metabolic abnormalities with tissue biomarkers of preclinical vascular involvement.
Methods: Eighty-two healthy volunteers (45 men; age 46$\pm$9) underwent a glucose tolerance test and a euglycemic hyperinsulinemic clamp to estimate IS (M/I, i.e. M value normalized by FFM and mean plasma insulin). Metabolic parameters measured included fasting and 2-hour glucose and insulin, detailed lipid profile, leptin, adiponectin and hs-CRP. Vascular examination included carotid-femoral pulse wave velocity (PWV) and radiofrequency-based ultrasound (QIMT® and QAS®, Esaote), for IMT and local stiffness estimate (beta index, BI). Acoustic properties of carotid wall were evaluated by videodensitometry and described as mean grey levels (MGL).
Results: in multiple regression models adjusted for sex and smoking, IMT was independently related directly to age and carotid diameter, and inversely to adiponectin (R2=0.34), IMTmax to age, systolic BP and adiponectin (R2=0.35), and carotid MGL to age and adiponectin (directly and inversely, respectively; R2=0.30). BI was related to age and M/I (directly and inversely, respectively; R2=0.44) and carotid-femoral PWV to age and glucose (directly; R2=0.39).
Conclusions: metabolic factors related to IR influence structure and function of carotid artery behind the main role of age. Adiponectin has an independent effect on carotid structure, while IS and plasma glucose mainly influence carotid and aortic stiffness.

P9.2
VASCULAR ADAPTATIONS TO BODY SIZE AND COMPOSITION IN ADOLESCENTS

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Background: increase in body mass index is accompanied by metabolic alterations but also by increased stroke volume (SV). Therefore, associated changes in vascular structure and function can not reflect only preclinical atherosclerosis but physiologic adaptation to body composition-related hemodynamic changes.
To evaluate the relationships between body composition and arterial structure and function without the influence of atherosclerotic risk factors, we assessed carotid intima-media thickness (IMT), luminal diameter (LD), wave speed (WS) and local pulse pressure (cPP)by radio-frequency based ultrasound (QIMT® and QAS®, Esaote), in 80 healthy children-adolescents with wide range of age (8-16 years) and BMI (15-40 kg/m2). Body composition was assessed by bioimpedance, visceral fat (VF) by ultrasound, and SV by Doppler. Plasma lipids, glucose and insulin were determined.
Results: body weight (BW) and fat free mass (FFM) were related to IMT (r=0.61 and 0.50), LD (r=0.54 and 0.53), WS (r=0.43 and 0.56) and cPP (r=0.36 and 0.49); fat mass (FM) was related to IMT and LD (r=0.40 and 0.29), and VF to IMT (r=0.41). SV was more strongly related to FFM than to FM (r=0.70 and 0.24). In multivariate models, IMT was determined by BW and triglycerides (R2=0.44), LD by BW and male sex (R2=0.37), WS by FFM and systolic BP (R2=0.39), cPP by FFM (R2=0.24). When SV was included into the models, it replaced FFM in model of cPP. Conclusion: adiposity-related changes in carotid function are depending on FFM-related increase in SV. Changes in carotid geometry also reflect an increase in body fat and plasma lipids.

P9.3
LOWER SUBENDOCARDIAL VIABILITY RATIO IN DIABETIC WOMEN—CONTRIBUTING TO THE ABROGATED CARDIOPROTECTIVE EFFECT OF FEMALE GENDER IN DIABETES?

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The cardioprotective effect of female gender is abrogated in the presence of type 2 diabetes, and female diabetic patients thus face comparable cardiovascular risk as men with type 2 diabetes. The SubEndocardial Viability Ratio (SEVR) is an index of myocardial oxygen supply and demand that can be assessed non-invasively by applanation tonometry. We hypothesized that diabetic women would have lower SEVR than diabetic men and non-diabetic subjects independently of conventional risk markers and arterial stiffness.