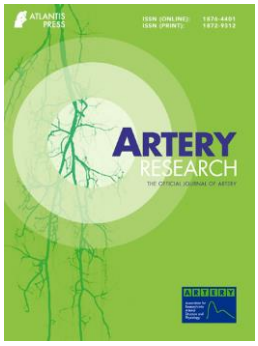

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P1.3: A NEW DYNAMIC ORGAN BATH SETUP TO ASSESS ISOBARIC STIFFNESS PARAMETERS OF PERIODICALLY STRETCHED ISOLATED MOUSE AORTIC SEGMENTS

Arthur J.A. Leloup*, Cor E. Van Hove, Guido R.Y. De Meyer, Dorien M. Schrijvers, Gilles W. De Keulenaer, Paul Fransen

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ARTERY 2015: Poster presentation abstracts

P1.1
PHYSICAL ACTIVITY IS ASSOCIATED WITH FLOW-MEDIATED DILATATION IN FEMALES

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Impairment of vascular endothelial function is an early sign of atherosclerosis. An active lifestyle is suggested to be positively associated with favorable endothelial function as opposed to a sedentary lifestyle.
The aim of this ongoing study (*Lifestyle, Biomarkers and Atherosclerosis Study*) is to investigate associations between vascular endothelial function and physical activity level in 1000 non-smokers without know disease aged 18-25 years. Preliminary data from the 317 first subjects with complete data will be reported here.
Flow-mediated dilation was assessed in *a. brachialis* by high-resolution ultrasound (Vivid e9) before and after 5-minutes occlusion, and time spent active (at moderate or vigorous intensity level) or sedentary was assessed by accelerometry (ActiGraph wGT3X-BT).
Females
n=226
Males
n=91
Gender differences
(*P*-value)
Age
BMI
Body fat (%)
Time spent active (min/day)
Time spent sedentary (min/day)
Flow Mediated Dilatation measures
Diameter, pre-stas (mm)
Increase, post-stas (mm)
Increase, post-stas (%)
21,8
22,4
27,8
45
514
3,16
0,28
8,9
21,8
22,9
15,0
45
524
3,74
0,28
7,5
1,00
0,14
<0,001
0,99
0,32
<0,001
0,96
<0,001
Multiple regression analyses show that time spent active is statistically associated with diameter increase (mm) and percentage increase (adjusted for pre-stas diameter) in females (beta coefficient = 0,144; p=0,032 and beta-coefficient=0,135; p= 0,041, respectively) but not in males. Time spent sedentary did not show any associations with the flow-mediated dilatation variables in neither females nor males.
In conclusion, already in young adulthood, an active lifestyle is associated with higher flow-mediated dilatation as a measure of endothelial function.

P1.2
NANOMECHANICAL ALTERATIONS IN THE ADVENTITIAL LAYER OF THE INTERNAL MAMMARY ARTERY OF PATIENTS WITH HIGH PWV

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Aim: Arterial stiffening occurs as part of the natural ageing process, and is thought to be related to the accumulation of collagen and degradation of elastin. However, little is known about how regional variations in arterial structure and mechanical properties contribute to arterial stiffening. This study compared localised differences in the nano-structure and mechanical properties in the internal mammary arteries (IMA) from patients with high and low PWV.
Methods: 6 IMAs were collected from coronary bypass operations and the patients were grouped according to their carotid-femoral PWV; high (14.6 ± 1.4 m/s) and low (8.7 ± 0.5 m/s). The nano-topography and elastic modulus were determined by atomic force microscopy (AFM) using 5 μm cryosections. Data are presented as means ± SEMs.
Results: Overall, IMAs in the high PWV group were significantly stiffer than in the low PWV group (High; 2234.7 ± 72.3 MPa, Low; 2015.3 ± 58.4 MPa), ($p < 0.0001$). Although no significant difference was found in the intimal or medial layers, the adventitia was stiffer in the high PWV group (High; 2597.6 ± 135.7 MPa, Low;2215.6 ± 110.2 MPa), ($p < 0.001$). Furthermore, the collagen fibrils in the adventitia of the high PWV group were found to have a smaller diameter (High; 118.44 ± 1.1 nm, Low; 123.81 ± 1.3 nm), ($p < 0.01$)).
Conclusion: Overall, the nanomechanical data associates with PWV data. The high PWV group exhibited higher nanomechanical stiffness alongside morphological alterations within the adventitial layer.

P1.3
A NEW DYNAMIC ORGAN BATH SETUP TO ASSESS ISOBARIC STIFFNESS PARAMETERS OF PERIODICALLY STRETCHED ISOLATED MOUSE AORTIC SEGMENTS

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Cyclic stretch is a major contributor of vascular function. However, isolated mouse aortas are frequently studied at low stretch frequency or even

isometric conditions. Pacing experiments done in rodents and humans show that arterial compliance is highly cyclic stretch frequency-dependent. The Rodent Oscillatory Tension Set-up to study Arterial Compliance (ROTSAC) is an in-house developed organ bath that clamps aortic segments (width 2mm, diameter 0.5-3mm) to imposed preloads at physiological rates up to 600bpm. The technique enables us to acquire pressure-diameter loops (derived from simultaneous force-displacement measurements) and calculate biomechanical parameters such as Peterson's modulus (Ep) and compliance. To our knowledge, this is the first set-up that facilitates the study of active vessel wall components, physiological stretch frequency and pressure variations and its effect on the biomechanical properties of the aorta.
Arterial stiffness is generally considered to be determined mainly by structural components. However, using this device, we were able to show — by isobaric determination of compliance and Ep while changing pressure and vascular smooth muscle cells (VSMCs) tone — that active vessel wall components are highly important in determining biomechanical properties of the aorta. Ep values for WT mouse aorta (350.3 ± 8.2 mmHg) were in accordance with literature data and increased 29% upon a rise in diastolic pressure of 40 mmHg, while isobaric Ep increased 47% upon maximal contraction of the VSMCs. We believe that this set-up can significantly contribute to a better understanding how active vessel wall components influence arterial stiffening, hypertension and its associated cardiovascular complications.

P1.4
HEMODYNAMICS OF PULMONARY HYPERTENSION: APPLICATION OF THE RESERVOIR-WAVE APPROACH

Anukul Ghimire [1,*], Mads Andersen [2,3], Lindsay Burrowes [1], J. Christopher Bouwmeester [4], Andrew Grant [1], Israel Belenkie [1], Nowell Fine [1], Barry Borlaug [3], John Tyberg [1]
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[3]*Mayo Clinic, Rochester, MN, USA*
[4]*Yale University, New Haven, CT, USA*

Using the reservoir-wave approach, previously we characterized pulmonary vasculature mechanics with multiple interventions in a canine model. In the present study, we measured high-fidelity pulmonary arterial (PA) pressure, Doppler flow velocity, and pulmonary capillary wedge pressure in 11 patients referred for evaluation of exertional dyspnea. The analysis was performed using the reservoir-wave approach; wave intensity analysis was subsequently utilized to characterize the PA wave pattern. Our objective was to identify specific abnormalities associated with pulmonary hypertension.
Seven patients with varying PA pressures had reduced pulmonary vascular conductance (i.e., the amount of flow that the lungs can accept per pressure gradient), suggesting that these patients might benefit from pulmonary vasodilator therapy, some even in the absence of markedly elevated PA pressures.
Right ventricular (RV) performance was assessed by examining the work done by the wave component of systolic PA pressure. Wave work, the non-recoverable energy expended by the RV to eject blood, varied directly with mean PA pressure. Wave pressure was partitioned into two components: forward-travelling and reflected backward-travelling waves. Among patients with lower PA pressures, we found pressure-decreasing backward waves that aided the RV during ejection, as previously reported in normal experimental animals. Among patients with higher PA pressures, we detected pressure-increasing backward waves that impede RV ejection.
We conclude that it is important to measure pulmonary vascular conductance to properly assess the pulmonary vasculature. The reservoir-wave approach and wave intensity analysis may prove to be valuable tools to evaluate RV performance and may facilitate development of therapeutic strategies.

P1.5
AGE AND HYPERTENSION STRONGLY REDUCE AORTIC VISCO-ELASTIC PROPERTIES IN RATS AT BASAL AND MATCHED BLOOD PRESSURE LEVELS

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Age and hypertension are major causes of large artery stiffening, a cardiovascular risk factor for heart and kidney damage. Long term hypertension induces vascular remodeling, accelerating vascular aging. The aged Spontaneously Hypertensive Rat (SHR) model is recognized for human cardiovascular pathology but discrepancies are apparent in studies of arterial stiffness.
We performed experiments using a robust aortic visco-elasticity analysis via echotracking in 20 (n=6) and 80 week old SHR (n=8), and respective control Wistar Kyoto rats (WKY, n=6-6) at basal and matched levels of blood pressure (BP). After anesthesia (pentobarbital), abdominal aortic diameter and pressure were recorded and BP was decreased by clonidine i.v. At basal BP, aortic pulse distension, compliance, distensibility (AD) and wall viscosity (AWV) were reduced and stiffness index increased with age and hypertension and further altered with age + hypertension. BP being adjusted to 130 and 100 mmHg between groups, there was no difference between 20w old SHR and WKY but importantly the age effect was maintained in both WKY and SHR and accentuated by hypertension in old rats. At 130 mmHg, AD = 24.2±1 in 20w WKY, 20.3±1.8 in 20w SHR, 12.4±1.3 in 80w WKY and 6.1±0.7 in 80w SHR; AWV = 58±5, 58±9, 29±1 and 10±2 in the same groups.
In conclusion reduced distensibility i.e. stiffening due to age is clearly shown here in both WKY and SHR as well as the effect of hypertension in aged rats. It will allow new investigations of the mechanisms and possible effect of drugs on aortic stiffness.

P1.8
DEVELOPMENT OF A TECHNIQUE FOR DETERMINATION OF PULMONARY ARTERY PULSE WAVE VELOCITY IN HORSES

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Calcification of the tunica media of the main pulmonary arteries has been observed in a large proportion of young racehorses. In humans, medial calcification is the most important cause of increased arterial stiffness, and has been implicated in the pathogenesis of microvascular diseases. Pulse wave velocity (PWV) is a marker of arterial stiffness. This study aimed to develop a technique for determination of pulse wave velocity of the main pulmonary arteries of horses.
Six healthy adult horses were sedated, and continuously monitored with electrocardiography during the procedure. The pulmonary artery (PA) trunk was cannulated via right heart catheterization, with a catheter introducer sheath (9Fr x 100cm). Introducer placement was guided with echocardiography. A custom-made dual pressure sensor catheter (PSC) (7Fr x 170cm) was inserted through the introducer sheath, and into one of the main branches of the PA. The position of the PSC in one of the main branches of the PA was confirmed with thoracic radiography and pressure measurements were recorded. The time delay of the pulse waves between the two sensors was used to calculate PWV.
The PSC placement was successfully achieved in all horses (6/6), without significant complications, aside from transient arrhythmias. The catheter was more commonly located on the left PA (5/6). The mean (±SD) PWV was 3.0±1.3m/s.
This study demonstrated the feasibility of a technique to determine PA-PWV in standing horses. The technique developed may allow further investigation of the effect of calcification of large pulmonary arteries in the development of microvascular disorders in horses.

P1.9
PLATELET-LOCALIZED FXI PROMOTES A GLYCOPROTEIN IBα DEPENDENT FEEDBACK LOOP IN ARTERIAL HYPERTENSION AND VASCULAR INFLAMMATION

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Background: Interactions of platelets, leukocytes and the vessel wall play pivotal roles in activating coagulation and precipitating thrombosis. High levels of angiotensin II (ATII) cause arterial hypertension by a complex inflammatory pathway requiring leukocyte recruitment and reactive oxygen species production within the vessel wall.
Objective: The aim of this work was to explore the role of platelet glycoprotein Ibα dependent thrombin-FXI feedback loop in arterial hypertension.
Methods: FXII-/-, FXI-/-, and hIL-4R/Ibα mice and 5/6 nephrectomized rats were used for this study. Mice where treated with ATII (1mg/kg^{-1}/d-1 for 7