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

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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 a mouse 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 wall components influence arterial stiffening, hypertension and its associated cardiovascular complications.

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

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Using the reservoir-wave approach, previously we characterized pulmonary vascular 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 pressure. 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±1.1 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±5, 58.9±5, 29.1±11 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 echocardiography 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±1.3 cm/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 Ib×-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 Ib× dependent thrombin-FXI feedback loop in arterial hypertension.

Methods: FXII/-, FXI/-, and hlL-4R/ib× mice and 5/6 nephrectomized rats were used for this study. Mice where treated with ATII (1mg/kgd/-1 for 7
Abstracts

P1.10 PULSE PRESSURE IN RELATION TO 24-HOUR URINARY SODIUM EXCRETION IN A SAMPLE OF HIGH-SALT INTAKE POPULATION

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Objectives: In recent years, many studies emphasized the role of arterial rigidity in the development of cardiovascular diseases. Pulse pressure in an easy-obtained, reproducible marker of arterial stiffness and an independent cardiovascular risk factor. On the other hand it was observed that sodium restriction could improve large elastic artery compliance. The aim of the study was to investigate the relation between salt intake and pulse pressure in high salt intake population.

Methods: The study group included 303 subjects recruited from the general population of Southern Poland. Ambulatory blood pressure (ABP) monitors (SpaceLabs 90207) were programmed to obtain measurements every 15 min. during the day and each 30 min. nighttime. Based on the ABP data, we calculated pulse pressure (PP) over 24h, daytime and nighttime. Sodium intake was assessed based on 24h urinary sodium excretion. Database management and statistical analysis were performed with SAS software.

Results: The study group included 163 men and 167 women, with 165 hypertensive individuals, 105 of them on antihypertensive treatment, mean age = 47.1 ± 15.7 yrs. While adjusting for age, sex, body mass index, 24h blood pressure, antihypertensive treatment, and lifestyle, we observed positive relation between daily sodium intake and 24h and daytime PP ([beta(SE): 0.016 ± 0.006 = 0.007], daytime PP ([beta(SE): 0.011 ± 0.005, p = 0.029] and non-significant trend regarding nighttime PP ([beta(SE): 0.009 ± 0.005, p = 0.094]).

Conclusion: In our high salt intake population, sodium intake was positively related to calculated pulse pressure over 24h and daytime.

P1.11 SOLUBLE IL-6 RECEPTOR CONCENTRATIONS ARE ASSOCIATED WITH AUGMENTATION INDEX IN HEALTHY YOUNG MALES

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Background: Augmentation Index (Alx) is considered a sensitive marker of arterial stiffness in young individuals. Increased levels of inflammatory markers such as interleukin-6 (IL-6) are associated with increased levels of arterial stiffness in older and diseased populations. However, little is known about these associations in young healthy individuals, as concentrations are prone to fluctuation. Data suggests that increased levels of the soluble IL-6 receptor (sIL-6R) facilitate the detrimental pro-inflammatory signalling of IL-6, which may highlight sIL-6R’s role as a mediator of chronic inflammation and associated disease states. Therefore, the aim of the study was to determine the associations between sIL-6R and IL-6 with Alx in a young healthy cohort.

Methods: In 20 healthy male subjects (age 22 ± 3 years), self-reported physical activity levels (PA) were determined via International Physical Activity Questionnaire. Peripheral and central blood pressure and Alx were measured using the Mobil-O-Graph system (IEM). Plasma concentrations of sIL-6R and IL-6 were assessed via enzyme-linked immunosorbert assay (R&D systems).

Results: Alx was significantly associated with levels of sIL-6R (r = 0.5, P = 0.02) but not associated with levels of IL-6 or PA (P > 0.05).

Conclusion: These novel pilot data suggest that elevated concentrations of sIL-6R at an early age may be indicative of an underlying vulnerability to inflammation-associated vascular stiffening. Furthermore, the absence of any association between IL-6 and Alx in our study implies that sIL-6R may be a more suitable biomarker than IL-6 for use in understanding the mechanisms by which inflammation affects vascular stiffening. However, larger studies are required to confirm our findings.

P1.12 IN IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION ARTERIAL NARROWING IS LIMITED AND HETEROGENEOUS

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Rationale: In severe idiopathic pulmonary arterial hypertension, iPAH, pulmonary vascular resistance is increased due to remodeling of the small (resistance) arteries. Most information on arterial remodeling is limited to assessments of increased wall thickness. Quantitative information on the number of arteries affected and their internal diameter decrease in relation to vessel size is limited. Our objective was therefore to quantify numbers of affected small arteries and their internal diameter decrease for the differently sized vessels.

Methods: Internal and external arterial diameters were measured in 5 controls and 6 iPAH subjects. Resistance arteries (13 to 500 µm) were classified in Strahler orders (1-8), and the number of fraction of affected vessels and their internal diameter decrease calculated.

Results: In iPAH not all resistance arteries are affected, on average about 70% of arteries have diameters not different from the control subjects, with the number of affected arteries varying between 20 and 50%. Within each order the diameters of affected vessels vary greatly and are decreased to 70-20% of control with on average to about 60% of control. We conclude that narrowing of resistance arteries a feature of iPAH and is heterogeneous: not all arteries are narrowed, and internal diameters of narrowed arteries, even within single orders vary largely. Determination of total vessel numbers of arteries and of veins is necessary to gain insight into the possible role of rarefaction and of changes in the venous system.

P1.13 CHANGES IN PULSE WAVE VELOCITY ALONE CANNOT PREDICT THE PULSE PRESSURE INCREASE WITH AGE

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Recently Weber et al. invasively obtained aortic Pulse Wave Velocity (PWV) as a function of age, [1] Systolic and diastolic arterial pressure were determined as well. PWV can be used to derive total arterial compliance, Ctot, as Ctot = k/PWV². With Ctot and Stroke Volume (SV), aortic Pulse Pressure (PP) can be approximated from Ctot = SV/PP. However, the PWV-derived value for Ctot predicted a larger PP increase with age than measured. [1] PWV increased from 5.6 to 12m/s between age Cao decreases to 0.6/4.6. Setting Ctot equal to Cao, PP would increase by the same factor, 2. However, the PWV-derived value for Ctot predicted a larger PP increase with age than measured. [1] PWV increased from 5.6 to 12m/s between age Cao decreases to 0.6/4.6. Setting Ctot equal to Cao, PP would increase by the same factor, 2. However, the PWV-derived value for Ctot predicted a larger PP increase with age than measured. [1] PWV increased from 5.6 to 12m/s between age Cao decreases to 0.6/4.6. Setting Ctot equal to Cao, PP would increase by the same factor, 2. However, the PWV-derived value for Ctot predicted a larger PP increase with age than measured.