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


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days) using osmotic minipumps. Blood pressure was recorded using tail cuff measurement and telemetry carotid implants. Vascular reactivity was assessed in isolated aortic segment, and thrombin generation was measured using calibrated automated thromboigraphy.

Results: ATII induces an upregulation of tissue factor, thrombin-dependent endothelial cell VCAM-1 expression and integrin a4- and platelet-dependent leukocyte adhesion to arterial conductance vessels. The resulting vascular dysfunction unexpectedly involved the activation of FXI but not FXII. The platelet FXI receptor glycoprotein Ibα supports the upregulation of thrombin feedback activation in ATII-treated mice. Importantly, pharmacologic inhibition of FXI synthesis is sufficient to prevent thrombin propagation on platelets, to reduce vessel wall leukocyte infiltration, and to diminish ATII-induced endothelial dysfunction and arterial hypertension in mice and rats.

Conclusion: Our results reveal a critical role of platelet GP Ibα to promote localized thrombin amplification and a FXI-thrombin feedback loop in ATII-induced vascular inflammation. Targeting FXI could be a novel therapeutic possibility to interrupt this heterotropic cellular coagulation-inflammatory circuit.

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 each 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 136 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 sodium intake and PP (β: 0.016 ± 0.006, p = 0.0075), daytime PP (β: 0.011 ± 0.005, p = 0.029) and non-significant trend regarding nighttime PP (β: 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 (Aix) 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 Aix 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 Aix@75 were measured using the Mobil-O-Graph system (IEM). Plasma concentrations of sIL-6R and IL-6 were assessed via enzyme-linked immunosorbent assay (R&D systems).

Results: Aix@75 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 Aix 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 averaged increases in 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 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 aortic 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 40 and >80 years of age thus aortic compliance (Ctot) decreased by a factor (12/5.6)² = 4.6. [1] Setting Ctot equal to Cao, PP would increase by the same factor, while measured PP increased from 50 to 90 mmHg. SV decreasing with age may play a role but certainly not a factor 2.

We hypothesize that Ctot is not equal to Cao as calculated form PWV: compliance of the conduit arteries, Cao, also contribute. This can be seen as follows. In the young Cao = 0.6, Cao = 0.35 and Cao = 0.25 (cgs units). At high age Cao reduces to 0.6/4.6 = 0.076 and Cao to 0.25/1.2 = 0.20, thus Cao = 0.28; about halved. PP then approximately doubles, in agreement with the pressure data. In aging Ctot decreases considerably less than Cao since the relatively smaller changes in Cao play a role as well. Changes in aortic PWV alone cannot predict the PP increase as a function of age.