P1.59: CHARACTERISTIC IMPEDANCE IN ISOLATED MOUSE LUNGS IS INVERSELY PROPORTIONAL TO PROXIMAL ARTERY STIFFNESS

D.M. Tabima Martinez, R.R. Vanderpool, N.C. Chesler


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role of arginase pathway in response to shear stress has never been investigated.

Methods: To evaluate the regulation of arginases by different shear stress patterns without neuroendocrine factors, we perfused carotid arterial segments for 3 days to unidirectional high and to low oscillatory shear stress hemodynamic conditions. We compared these well-controlled measurements to an in vivo model of shear stress-induced atherogenesis. Vasoreactivity, immunohistochemistry and Western blot were used to characterize the role of arginase pathway.

Results: Our results from ex vivo perfusion arteries showed for the first time that exposure of carotid to oscillatory flow significantly increase arginase II protein expression and activity as compared to high shear stress flow conditions (athero-protective). Our data suggested that arginase I and II are also differentially modulated in mice chronically treated with arginase inhibitor, nor-L- hydroxy-nor-L-arginine for 9 weeks (10mg/kg/day, i.p).

Conclusions: The present study demonstrates that arginase expression is already modulated by 3 days exposure to different shear stress patterns in carotid arteries perfused ex vivo. Similar findings are also observed in a model of shear stress-induced atherogenesis in vivo.


P1.58
ABNORMAL VASCULAR FETAL PROGRAMMING IN RATS SUBJECTED TO MATERNAL DIABETES
C. Fassoï1, J.P. Duong Van Huyen1, C. Labat2, C. Perret1, P. Barbry3, P. Lacolley1, M. Lelièvre-Pégorier1, S. Laurent1, M. Lelie`vre-Pe`gorier1, S. Laurent1, 1 INSERM U872, Université Paris 5, UPMC, HEGP, Paris, France 2 INSERM UMR8684, Nancy, France 3 CNRS UMR 6097, Sophia-Antipolis, France

Epidemiologic studies have clearly identified modifications of fetal environment as a risk factor for the development of cardiovascular diseases in adulthood. In our experimental model, rats exposed in utero to maternal diabetes develop an hypertension as early as 6-month of age. In order to determine if the development of this hypertension results from an abnormal vascular fetal programming, gene expression profile of the aorta was studied on oligonucleotides chips (Agilent, G4130, 22k). Arterial structure and elastic properties were assessed on 3-non-hypertensive stage) to 18-month-old rats from control (CMO3 and CMO18) and diabetic mothers (DMO3 and DMO18), with echo-tracking device and histomorphometry. DMO had a significantly higher SBP than CMO at 6 and 18 months of age (DMO18: 218±3 mHg vs CMO18: 155±2 mHg). DMO3 are characterized by an over-expression of subunits of P450 (Cyp4f4, Cyp4f2, Cyp4b1) and an under-expression of pros-tacyclin receptor, which both could contribute to vasoconstriction. Carotid elastic properties were not significantly different between CMO and DMO at 3 and 6 months. Surprisingly, thoracic aorta of DMO was not significantly thicker than CMO at 6 and 18m, in spite of the higher level of SBP in DMO. The lack of BP-induced wall thickening in DMO can be related to the under-expression of genes coding for proteins involved in migration and cell-matrix interaction (Evl, Ckap4, Dcamk1). In conclusion, these results suggest an abnormal vascular fetal programming in rats exposed in utero to maternal hyperglycemia, which could explain the structural and functional arterial disorders observed in this model.

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P1.59
CHARACTERISTIC IMPEDANCE IN ISOLATED MOUSE LUNGS IS INVERSELY PROPORTIONAL TO PROXIMAL ARTERY STIFFNESS
D.M. Tabima Martinez, R.R. Vanderpool, N.C. Chesler. University of Wisconsin, Madison, WI, USA

Impedance is a complex and comprehensive function of hemodynamics that can be measured in vivo and from which certain metrics, including input impedance (\(Z_i\)), first harmonic impedance (\(Z_1\)) and characteristic impedance (\(Z_c\)), can be calculated. According to lumped-parameter models of intact human lungs, \(Z_1\) is proportional to proximal artery (PA) stiffness and \(Z_c\) is directly proportional to PA stiffness and inversely proportional to size. Our goal was to investigate how these metrics of impedance are related to PA stiffness in isolated mouse lungs.

Sinusoidal pressure-flow tests in isolated lungs and static pressure-diameter tests in isolated PAs from inbred mice were performed after exposure to zero days (CTL) or ten days of hypoxia (HPH). To normalize mean PA pressure in isolated lungs, measurements were taken with and without vasodilatation (Y27632, 1X10-5 M).

In PAs, the incremental elastic modulus (\(E_{inc}\)) increased with HPH (P<0.05); no differences in size were significant. In lungs, \(Z_1\) increased (P<0.0001) but \(Z_c\) decreased (P<0.05) with HPH while mean PA pressure (and \(Z_a\)) increased (P<0.0001). When measured at the same pressure (and \(Z_a\)), \(Z_1\) returned towards CTL values (P=0.10 vs. CTL) but \(Z_c\) remained decreased (P<0.0001). Under these conditions, PAs were still stiffer than CTL (P<0.0005) and slightly but not significantly larger (P=0.051).

Overall, \(Z_1\) was sensitive to pressure-induced dilation and strain stiffening in PAs but \(Z_c\) was additionally sensitive to HPH-induced stiffness. In contrast to intact human lungs, our results suggest that in isolated mouse lungs \(Z_c\) is inversely proportional to PA stiffness.


P2.01
LONGITUDINAL STUDY OF VASCULAR MARKERS OF PREMATURE ATHEROSCLEROSIS IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS
T.J. Bradley, P.N. Tyrrell, C. Slorach, L. Ng, L.A. Nukumizu, C.A. Boros, S.M. Benseler, E.D. Silverman. The Hospital for Sick Children, Toronto, Canada

Background: Patients with pediatric Systemic Lupus Erythematosus (pSLE) are at increased risk of premature atherosclerosis irrespective of exposure to traditional cardiovascular risk factors. The goals of this study were to determine the progression of vascular markers of premature atherosclerosis in a prospectively followed pSLE cohort and the role of treatment and disease activity related factors.

Methods: At baseline and first follow-up drug therapy and disease activity were recorded, fasting lipid and glycolic profiles performed; and vascular markers including intima-media thickness (CIMT), flow-mediated dilatation (FMD), and pulse wave velocity (PWV) assessed. Differences between baseline and follow-up time points were tested as paired measures adjusted for time and compared in univariate analysis.

Results: Forty-three pSLE were assessed at baseline (age 14.0±2.8 years; disease duration 2.3±2.8 years, 81% female) and follow-up (1.6±0.5 years later). No overall difference was observed in CIMT (0.01±0.05 mm, P=0.15), FMD (0.19±0.5 %, P=0.81) and PWV (0.15±0.1 m/sec, P=0.39). When considering the time-dependent effects of treatment and disease activity on these vascular markers, corticosteroid use was found to be negatively associated with CIMT at follow-up (r=-0.44, P=0.004) and remained significant in a multiple variable model (R2=0.63, P<0.001).

Conclusion: In pSLE of relatively short duration, progression of vascular markers of premature atherosclerosis was not observed over short-term follow-up, but change in CIMT was found to be negatively associated with the amount of corticosteroid use. This suggests aggressive immunotherapy may reduce the atherogenic burden of chronic inflammation in pSLE and warrants further investigation.

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P2.02
IMPACT OF RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS ON ARTERIAL WALL STIFFNESS
A. Cypiene1, A. Venalis1, J. Dadonie1, R. Rugiene1, L. Ryliskyte2, Z. Petruniolenie2, M. Kovaite2, V. Skorniakov2, A. Laucevicius2. 1 Institute of Experimental and Clinical Medicine, Vilnius University, Vilnius, Lithuania 2 Department of Cardiovascular Medicine, Vilnius University, Centre of cardiology and Angiology, Vilnius University Hospital Santariskiu klinikos, Vilnius, Lithuania

Background: There was demonstrated that rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) were associated with arterial damage. However it is not well known which of diseases has bigger impact on measures of arterial stiffness.

Aim of the study: was to assess whether aortic augmentation index (Aix) is modified in middle age RA and SLE women and to evaluate which one of these diseases has a greater influence on the parameter.

Methods: We examined 63 RA (age 41.48±10.77 years) with high disease activity (DAS28 5.49±0.92), 31 SLE (age 37.23±9.09) with moderate disease.