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# LAA1: HEMODYNAMIC AND STRUCTURAL ARTERIAL PARAMETERS' ASSOCIATION WITH INTERINDIVIDUAL VARIATIONS OF BODY MASS INDEX IN CHILDHOOD AND ADOLESCENCE

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in systolic/diastolic BPs and pulse pressure averaged 11.8/−1.6, 12.7/−1.8 and 10.3/−1.2 mmHg and 13.4, 14.4 and 11.5 mmHg, respectively ( $P < 0.0001$ ). Cornell voltage and index averaged 1.18 mV and 114.8 mV × ms. The Cornell voltages were 0.104/0.086 and 0.082/0.105 mV higher in relation to brachial 24-h and asleep systolic/diastolic BP (per 1-SD), respectively, and 0.088/0.90 mV and 0.087/0.107 mV higher in relation to central BP. The corresponding estimates for the Cornell indexes were 9.6/8.6 and 8.2/105 mV × ms peripherally and 8.6/8.9 and 8.8/10.7 mV × ms centrally. The regression slopes were similar for brachial and central BP ( $P \geq 0.054$ ). Associations of the ECG measurements with awake BP, PP, the augmentation ratio and pressure amplification did not reach significance.

**Results:** NIAGEN<sup>®</sup> safely and effectively raised circulating levels of NAD<sup>+</sup> and related metabolites. Although no effect was observed on endothelial function, NIAGEN<sup>®</sup> significantly lowered PWV as well as systolic (SBP) and diastolic blood pressure (DBP) in all subjects ( $P < 0.05$ ). When separated by baseline BP status, the BP-lowering effect of NIAGEN<sup>®</sup> was observed in pre-hypertensive (pHTN,  $n = 13$ ) but not normotensive ( $N = 11$ ) individuals ( $P < 0.01$ ). Interestingly, NIAGEN<sup>®</sup> was lowered in all subjects regardless of baseline BP status.

**Conclusion:** Chronic NIAGEN<sup>®</sup> supplementation lowers SBP in pHTN older adults and reduces aortic stiffness, independent of baseline blood pressure status.

**Table** Association of ECG Cornell voltage and indexes with peripheral and central BP.

	Cornell voltage ( $S_{V3} + R_{aVL}$ , mV)				Cornell index (Cornell voltage × QRS duration, mV × ms)				
	Peripheral BP		Central BP		Peripheral BP		Central BP		
	Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P	
<b>Systolic BP</b>									
24-h	0.104 (0.016 to 0.191)	0.021	0.088 (0.0003 to 0.177)	0.049	9.61 (0.65 to 18.57)	0.036	8.58 (−0.40 to 17.56)	0.061	
Awake	0.086 (−0.001 to 0.175)	0.054	0.062 (−0.026 to 0.151)	0.17	7.69 (−1.30 to 16.69)	0.093	5.80 (−3.23 to 14.82)	0.21	
Asleep	0.082 (−0.006 to 0.170)	0.068	0.087 (−0.001 to 0.175)	0.053	8.17 (−0.82 to 17.16)	0.075	8.76 (−0.217 to 17.74)	0.056	
<b>Diastolic BP</b>									
24-h	0.086 (−0.002 to 0.174)	0.056	0.090 (0.002 to 0.178)	0.045	8.57 (−0.41 to 17.55)	0.061	8.93 (−0.04 to 17.90)	0.051	
Awake	0.056 (−0.032 to 0.145)	0.21	0.060 (−0.029 to 0.149)	0.18	5.62 (−3.42 to 14.65)	0.22	5.97 (−3.06 to 15.00)	0.19	
Asleep BP	0.105 (0.017 to 0.192)	0.020	0.107 (0.019 to 0.194)	0.017	10.53 (1.60 to 19.47)	0.021	10.71 (1.78 to 19.64)	0.019	
<b>Pulse pressure</b>									
24-h	0.040 (−0.049 to 0.129)	0.38	0.016 (−0.073 to 0.105)	0.72	3.07 (−5.99 to 12.13)	0.50	1.31 (−7.76 to 10.38)	0.77	
Awake	0.048 (−0.041 to 0.137)	0.29	0.012 (−0.077 to 0.101)	0.78	3.63 (−5.43 to 12.68)	0.43	0.68 (−8.40 to 9.74)	0.88	
Asleep	0.001 (−0.091 to 0.088)	0.98	0.001 (−0.087 to 0.090)	0.98	−0.29 (−9.37 to 8.78)	0.95	0.21 (−8.86 to 9.28)	0.96	

ECG refers to electrocardiography. BP stands for blood pressure. Cornell voltage is the voltage sum of S wave in precordial V3 lead ( $S_{V3}$ ) and R wave in limb aVL lead ( $R_{aVL}$ ), while Cornell index is the product of QRS duration multiplied by the Cornell voltage. The estimate (95% Confidence Interval, CI) of the association was unadjusted and expressed as 1-SD increase of BP. P value is for significance of the estimate. The association estimates of Cornell voltage ( $P \geq 0.054$ ) and index ( $P \geq 0.079$ ) with central BP were not significantly different from those estimates with peripheral measurements.

**Conclusions:** The diurnal rhythm of peripheral and central BP run in parallel. Central BP does not improve the association of Cornell voltage or index with peripheral BP.

#### Joint Session with LATAM and North American Artery

##### NAA1

#### NICOTINAMIDE RIBOSIDE SUPPLEMENTATION REDUCES AORTIC STIFFNESS AND BLOOD PRESSURE IN MIDDLE-AGED AND OLDER ADULTS

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**Purpose:** Regular calorie restriction (CR) improves endothelial function and lowers aortic stiffness in older mice and humans; however, adherence to sustained CR remains poor, and possibly unsafe in normal weight older adults. Nicotinamide adenine dinucleotide (NAD<sup>+</sup>) is an important signaling molecule involved in the beneficial effects of CR and we have recently demonstrated that boosting NAD<sup>+</sup> reverses these measures of arterial aging in older mice. The purpose of this study was to determine if supplementation with nicotinamide riboside (NIAGEN<sup>®</sup>; ChromaDex, Inc.), a naturally occurring precursor to NAD<sup>+</sup>, would similarly improve vascular function with aging in humans.

**Methods:** Healthy middle-aged and older adults (65 ± 2 yrs,  $n = 24$ ) received oral NIAGEN<sup>®</sup> (500 mg, 2x/day) and placebo capsules for six weeks each in a randomized, placebo-controlled crossover study. Blood pressure (BP), aortic stiffness (carotid-femoral pulse wave velocity [PWV]), and endothelial function, (brachial artery flow-mediated dilation [FMD]), were measured at the end of each intervention phase.

##### LAA1

#### HEMODYNAMIC AND STRUCTURAL ARTERIAL PARAMETERS' ASSOCIATION WITH INTERINDIVIDUAL VARIATIONS OF BODY MASS INDEX IN CHILDHOOD AND ADOLESCENCE

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**Background:** Several works analyze arterial parameters' (stiffness levels, wall thickness, etc.) association with variations of body mass index (BMI) in pediatric populations.

However, none integrate different arterial parameters as comparable continuous (standardized) variables, in order to assess their association with standardized (age- and sex-independent) BMI scores (zBMI).

**Aims:** To analyze the association of standardized arterial parameters with interindividual variations of zBMI.

**Methods:** 609 children and adolescents (mean age/range: 12/4–18 years, 45% females) were studied. Body mass index (BMI) was calculated. zBMI scores were derived from population-based tables. Non-invasive arterial assessment was performed: oscillometric measurements of peripheral systolic (pSBP), diastolic (pDBP) and pulse pressure (pPP), and central (applanation tonometry) systolic (cSBP), diastolic (cDBP) and pulse pressure (cPP); ultrasonographic measurements of common carotid (CCA), femoral (CFA) and brachial (BA) diastolic diameters (DD), and CCA intima-media thickness (cIMT). Arterial elastic moduli (EM) were calculated. Arterial parameters were standardized with equations derived from a reference population (no cardiovascular risk factor exposure). Simple linear regression models were obtained for the different standardized arterial parameters with zBMI as the independent variable. Statistical threshold was 0.05.

**Results:** We found a positive and significant association between zBMI and standardized pSBP ( $\beta = 0.210$ ), pPP ( $\beta = 0.150$ ), cSBP ( $\beta = 0.204$ ) and cPP ( $\beta = 0.188$ ), CCA DD ( $\beta = 0.145$ ), FCA ( $\beta = 0.143$ ), BA ( $\beta = 0.210$ ), cIMT ( $\beta = 0.135$ ), and CCA EM ( $\beta = 0.117$ ).

**Conclusions:** Higher zBMI associated higher standardized arterial blood pressure, stiffness levels, diameters and thickness. Hemodynamic parameters presented the stronger associations with zBMI variations.

## Oral session II – Young Investigator Session

### 2.1

#### COGNITION IN RELATION TO THE RETINAL MICROCIRCULATION IN CHILDREN BORN PREMATURELY OR AT TERM

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**Background:** The retinal microvasculature can be visualized noninvasively and mirrors the status of the cerebral vasculature. We therefore investigated in 93 prematurely born infants (birth weight < 1000 g) and 87 controls born at term whether neurocognitive performance at ~11 years is associated with the diameter of retinal microvessels.

**Methods:** We post-processed retinal photographs by a semi-automated software (Singapore I Vessel Assessment, version 3.6) and administered the Wechsler Non-Verbal test, Dutch version (Pearson, The Netherlands) to estimate the intelligence quotient (IQ) by combining matrix reasoning and spatial span.

**Results:** Compared with the controls, cases had lower IQ (92.5 vs. 108.7;  $P < 0.001$ ), smaller central retinal arteriolar (CRAE; 162.7 vs. 174.0 mm;  $P < 0.001$ ) and venular (CRVE; 234.7 vs. 242.7 mm;  $P = 0.003$ ) diameters and CRAE/CRVE ratio (AVR; 0.70 vs. 0.72;  $P = 0.002$ ) and lower body mass index (17.0 vs. 17.7 kg/m<sup>2</sup>;  $P = 0.044$ ), but higher mean arterial pressure (82.7 vs. 77.7 mmHg;  $P < 0.001$ ). In all children, the effect sizes associated with a 1-SD increase in CRAE were +3.87 ( $P < 0.001$ ), +1.80 ( $P = 0.004$ ) and +2.26 ( $P = 0.003$ ) for total IQ, matrix reasoning, and spatial span, respectively. In models adjusted for body mass index and mean arterial pressure, these estimates were +3.21 ( $P = 0.009$ ), +1.57 ( $P = 0.020$ ), and +1.84 ( $P = 0.024$ ), respectively. The associations of IQ and matrix reasoning with AVR also attained significance ( $P \leq 0.031$ ).

**Conclusions:** In conclusion, our findings suggest that underdevelopment of the microcirculation in prematurely born children might have lasting effects on their cognitive performance.

### 2.2

#### HEART STRUCTURE AND VASCULAR FUNCTION IN YOUNG PATIENTS AFTER ENDOVASCULAR REPAIR FOR BLUNT THORACIC AORTIC INJURY

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**Objective:** Thoracic Endovascular Aortic Repair (TEVAR) currently represents the gold standard of treatment for Blunt Thoracic Aortic Injury (BTAI). Nevertheless, there is an ongoing debate surrounding its safety and efficacy and its subsequent CV effects. The present study is aimed at assessing heart and aortic structure and function after TEVAR in BTAI patients

**Method:** In 20 patients (18 men, age  $41 \pm 14$  years) treated with TEVAR (11 Gore-CTAG, 9 Medtronic-Valiant) after BTAI, between 2004–2015, after a median follow-up time of 3 years (range 12–1 years; T1) we evaluated BP, cf-PWV (sphygmocor) and Left Ventricular Mass Index (LVMI) on echocardiography.

**Results:** At baseline, all the patients were normotensive; At T1 despite mean normal BP value ( $131 \pm 12/85 \pm 10$ ) 11 patients (55%) were hypertensives. Also LVMI ( $81,84 \pm 28,11$  g/m<sup>2</sup>) and PWV ( $7,58 \pm 1,48$  m/s) mean values were within the normal range. When patients were divided accordingly to the used graft patients treated with Medtronic-Valiant showed a significantly higher LVMI ( $97,17 \pm 35,78$  vs  $69,58 \pm 11,24$  g/m<sup>2</sup>;  $p < 0,05$ ) and PWV ( $7,78 \pm 1,74$  vs  $6,45 \pm 1,54$  m/s;  $p < 0,05$ ) compared with those treated with Gore-CTAG. Same figures were founded when patients were divided accordingly to the treating time with those treated more than 3 years before the evaluation that showed higher LVMI ( $91,16 \pm 34,73$  vs  $70,20 \pm 9,44$  g/m<sup>2</sup>;  $p < 0,01$ ) and PWV ( $7,50 \pm 1,98$  vs  $6,38 \pm 1,04$  m/s;  $p < 0,05$ ).

**Conclusions:** TEVAR for BTAI is associated after some years with the development of hypertension and heart and vascular alterations. The presence of TEVAR modify aortic functional properties and induce in young subject an increase in BP and LVMI probably related to the presence of a rigid aorta.

### 2.3

#### BIOMECHANICAL AND STRUCTURAL QUANTIFICATION OF VASCULAR DAMAGE: A UNIQUE INVESTIGATION OF STENT IMPLANTATION

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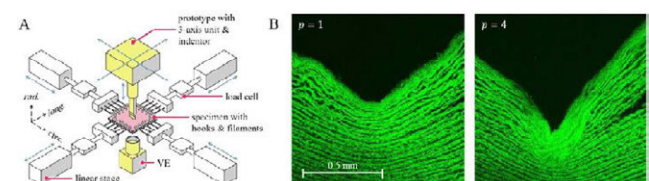
The most challenging complication after coronary stent implantation is in-stent restenosis [1], which is mainly caused by mechanically induced injuries due to overloading. From a biomechanical point of view, the processes occurring inside the arterial tissues during stent implantation (SI) is rather unknown.

This study shows a novel approach to quantify vascular damage due to SI a multi-scale examination of coronary arteries with generated injuries using a unique experimental in vitro setup.

The setup consists of a biaxial tensile testing stage to apply physiological loads on rectangular specimens of coronary arteries and a triple-axis-unit, which allows the indentation of stent struts into arterial tissues under a specified pressure (Fig. A). In addition, the multi-scale investigation of the mechanical and structural responses of the resulting lesion, following the protocol of Sommer et al. [2], is carried out by calculating Cauchy stresses and analyzing healthy and injured specimens with second harmonic generation (Fig. B) and electron microscopy.

The results indicate that the usually wavy collagen fibers straightened, compress and align around the lesion (Fig. B). In addition, the evaluation of the material characteristics reveals a significant softening of injured tissues. Fig. A: Design of the experimental setup, showing a biaxial tensile testing stage (white parts) and the triple-axis-unit for indentation tests (yellow parts).

Fig. B: Sectional view through the tissue perpendicular to the lesion. The SHG images show collagen fibers of specimens from a 6-months-old porcine descending aorta responding under different pressures (1 and 4 MPa).



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