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P155: CORRELATION OF SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS AND S100-A1 ON ARTERIAL STIFFNESS IN NORMOTENSIVE PATIENTS WITH DIABETES

Patricia Quezada Fernandez, Fernando Grover Páez, Becerra Ramos, Carlos, Jhonatan Trujillo Quiros, Walter Trujillo Rangel, Sánchez Rodríguez Sánchez Rodríguez, David Cardona Müller, Mayra Jimenez Cázarez

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EH (either newly diagnosed with high BP values or longer lasting), emphasizing on the need of early and effective glycemetic control.

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MARKER OF TYPE VI COLLAGEN FORMATION (PRO-C6) IS ASSOCIATED WITH HIGHER ARTERIAL STIFFNESS IN TYPE 1 DIABETES

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Aim: Arterial stiffening reflects fragmentation and loss of elastin fibers and accumulation of stiffer collagen fibers in the media of large arteries. We evaluated associations between carotid-femoral pulse wave velocity (cfPWV) and a marker of collagen type VI formation (Pro-C6) and a marker of collagen type III degradation (C3M) in type 1 diabetes.

Methods: Serum and urinary level of Pro-C6 and C3M was measured with ELISA in 634 patients with type 1 diabetes. cfPWV was assessed by the SphygmoCor device. We applied unadjusted and adjusted linear regression analyses. Adjustment included sex, age, mean arterial pressure, LDL cholesterol, smoking, HbA_{1c}, eGFR and urinary albumin excretion rate. To adjust for urine output levels, the urinary markers were normalized for urinary creatinine.

Results: Of the 634 patients, 349 (55%) were male, mean \pm SD age was 54.6 ± 12.6 years and cfPWV 10.4 ± 3.3 m/s.

Higher serum and urinary level of Pro-C6 was associated with higher cfPWV in unadjusted models ($p \leq 0.039$), after adjustment only higher serum level remained significantly associated with higher cfPWV (β estimate per doubling: 0.47 ± 0.21 ; $p = 0.028$).

Lower urinary level of C3M was associated with higher cfPWV in the unadjusted model ($p < 0.001$), but significance was lost after adjustment ($p = 0.44$). Higher serum level of C3M was associated with higher cfPWV in the unadjusted model ($p = 0.002$), but significance was lost after adjustment ($p = 0.34$).

Conclusion: In type 1 diabetes, higher serum levels of Pro-C6, a marker of collagen type VI formation, was associated with increased arterial stiffness. This observation could introduce a new target for therapeutic intervention.

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VASCULAR STRUCTURE AND FUNCTION IN RELATION TO WEIGHT EXCESS AND BLOOD PRESSURE IN A SAMPLE OF OBESE CHILDREN

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Objective: To investigate the influence of weight excess and blood pressure (BP) on vascular structure and function in a sample of obese children.

Methods: We measured office and ambulatory BP (ABPM), carotid intima-media thickness (cIMT), endothelial function by the Flow Mediated Dilation (FMD) technique, carotid distensibility (cDC) (ultrasonograph: LogiQ P5 Pro; software: Multimedia Video Engine II, DSP Lab, Pisa CNR, Italy) (1) and stiffness index (SI) by photoplethysmography (Pulce Trace PT1000, MicroMedical Ltd, UK) (2) in overweight and obese children (BMI > 90th percentile for sex and age).

Results: Seventy children with weight excess were enrolled (age 11.5 ± 2.4 years; female n: 30). cDC showed inverse correlation with BMI and waist circumference ($r_{\text{spearman}} = -0.403$ and $r_s = -0.346$, respectively), 24h-SBP ($r_s = -0.449$) and nighttime-SBP ($r_s = -0.490$). SI inversely correlated with BMI ($r_s = -0.359$) and waist/height ratio ($r_s = -0.303$). When comparing normotensive and hypertensive children, as defined on the basis of the

ABPM, no significant differences in vascular tests were found, although cDC tended to be lower in hypertensive. In normotensive subjects (n: 53) cIMT directly correlated with nighttime-SBP and DBP. Most of the correlations remained significant after adjustment for age, sex, BMI and BP.

Conclusions: These data suggest that arterial elasticity is negatively affected by weight excess and 24h-BP levels even in childhood. In the normotensive subgroup it is detectable an effect of BP also on arterial structure.

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CORRELATION OF SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS AND S100-A1 ON ARTERIAL STIFFNESS IN NORMOTENSIVE PATIENTS WITH DIABETES

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Background: Accumulation of advanced glycation end products (AGEs) are involved in several pathophysiological processes in the vessel wall, that may cause premature atherosclerosis and arterial stiffening (1). A soluble form of RAGE (sRAGE), which is a splice variant of full-length RAGE has been considered to be protective against diseases originating from RAGE activation since sRAGE can bind and sequester RAGE ligands and reduce RAGE activation (2). S100A1 is the most abundant calcium-binding protein in myocardial tissue and is a major determinant of cardiac function. This circulating ligand of the RAGE is known as a pro-inflammatory factor in diabetes. Aberrant expression levels of S100A1 surfaced as molecular key defects, driving the pathogenesis of cardiovascular diseases (3).

Objective: This study was design to explore the relationship between serum levels of sRAGE and S100A1 on arterial stiffness in non-hypertensive patients with diabetes.

Methods: Using a cross-sectional design, a total of 20 non-hypertensive patients with diabetes were recruited. A fasting blood sample, medical history and arterial stiffness parameters were collected.

Results: In bivariate analysis, sRAGE positively correlated with time evolution of diabetes ($r = 0.503$, $p < 0.024$) and negatively correlated with systolic ($r = -0.457$, $p = 0.043$) and diastolic blood pressure ($r = -0.527$, $p = 0.017$). S100A1 positively correlated with creatinine ($r = 0.724$, $p < 0.000$) and negatively correlated with peripheral and central hemodynamics, including augmentation index ($r = -0.469$, $p = 0.037$), as shown in Table 2.

Table 2. Correlation of sRAGE with metabolic, hemodynamic and arterial stiffening variables.

Variables	r Spearman	p-value
T2DM time evolution	-0.203	0.309
HbA1c	-0.082	0.780
Creatinine	0.724	0.000*
Systolic Blood pressure	-0.487	0.029*
Diastolic Blood pressure	-0.456	0.043*
Pulse pressure	-0.476	0.034*
Arterial Mean Pressure	-0.437	0.054*
Central Systolic Blood Pressure	-0.452	0.045*
Central Diastolic Blood pressure	-0.448	0.047*
Aortic Pulse Wave velocity	-0.361	0.118
Central pulse pressure	-0.035	0.041*
Aortic Augmentation Index	-0.469	0.037*

Abbreviation: sRAGE, soluble receptor for advanced glycation end products; T2DM, type 2 diabetes mellitus

Conclusion: This study shows a significant correlation of serum sRAGE and S100-A1 on peripheral and central hemodynamics in non-hypertensive diabetic patients.

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DURATION OF DIABETES MELLITUS IS A SIGNIFICANT PREDICTOR OF ARTERIAL STIFFNESS IN PATIENTS WITH ARTERIAL HYPERTENSION AND TYPE 2 DIABETES MELLITUS

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Background: Diabetic complications increase with disease duration but little is known about the relationships between aortic stiffness and diabetes duration.

Aim: to assess associations of diabetes mellitus (DM) duration and parameters of arterial stiffness in patients with arterial hypertension (AH) and T2DM.

Methods: 90 patients with AH and T2DM were included (39%males, mean age 63,8 ± 11,6 years, 44%smokers). Mean office BP was 146 ± 23/86 ± 10 mmHg. All patients received combined AHT, target BP < 140/85 mmHg was achieved in 52,7% of patients. Median duration of DM was 8,5 years (IQR 2; 13 years), mean glucose was 8,0 ± 2,4 mmol/l, mean HbA1c 9,2 ± 2,0%. BP was measured with a validated oscillometric device. Parameters of arterial stiffness were assessed by applanation tonometry, cardio-ankle vascular index (CAVI) and vascular age were measured (VaSera 1500). p < 0,05 was considered significant.

Results: Mean central BP was 132 ± 18/79 ± 12 mmHg, mean cfPWV -10,5 ± 2,4 m/s, mean R-CAVI-8,8 ± 1,9, L-CAVI-8,9 ± 1,8. Further analysis was performed in subgroups according to tertiles of DM duration (G1 < 4 years (n = 31), G2-4-10 years (n = 30), G3 > 10 years (n = 29)). Patients in G3 were older (69,5 ± 11,1 vs 62,1 ± 11,2 vs 60,0 ± 10,8 years), had higher vascular age (73,8 ± 9,0 vs 68,6 ± 11,8 vs 64,5 ± 13,4 years) and R-CAVI (9,3 ± 1,9 vs 9,0 ± 1,8 vs 8,1 ± 1,9); p < 0,05 for trend. Patients from G3 and G2 had the highest level of cfPWV compared to G1 (11,0 ± 2,0 and 11,4 ± 2,4 vs 9,1 ± 2,4 m/s, p = 0,0009). There were significant correlations between duration of DM and age (r = 0,35), vascular age (r = 0,30), creatinine (r = 0,23), cfPWV (r = 0,34), and R-CAVI (r = 0,3). Only age and DM duration were predictors of PWV increase (β = 0,3, p = 0,02 and β = 0,2, p = 0,04, respectively).

Conclusions: In diabetic patients, aortic stiffness is strictly correlated with diabetes duration, independently of blood pressure level and diabetes control.

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RETINAL ARTERIOLAR FUNCTION, ENDOTHELIAL DYSFUNCTION AND ARTERIAL STIFFNESS IN PATIENTS WITH TYPE 2 DIABETES

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Background: Crosstalk between large and small arteries has been suggested to partake in the microvascular complication development in patients with type 2 diabetes mellitus (T2DM). Yet, data are scarce.

In the present study, we aimed to elucidate the crosstalk between large and small arteries in T2DM.

Methods: Twenty patients with T2DM and 20 sex- and age matched controls were included. Arterial stiffness was assessed by carotid-femoral Pulse Wave Velocity (cfPWV) using the SphygmoCor. Endothelial function was assessed using EndoPAT. Retinal blood supply regulation was examined by retinal arteriolar diameter change during i) exposure to flickering lights, ii) isometric exercise (hand-weight lifting), and iii) a combined stimulus of i) + ii) using the Retinal Vessel Analyzer (RVA).

Results: T2DM patients had higher cfPWV than controls (9.3 ± 1.8 m/s vs. 8.3 ± 2.2 m/s, p = .049). No group difference was observed in endothelial function (0.71 ± 0.30 vs. 0.81 ± 0.30, p = .32) or in response to intervention with flicker, exercise or the combination (all p > 0.05). Endothelial function was associated with mean arteriolar diameter change for the combination intervention (Beta = 0.033 [0.0013; 0.064], p = .042) in patients and controls. No association was observed between cfPWV and retinal arteriolar %-diameter change in patients or controls.

Conclusion: Peripheral endothelial function was associated with retinal arteriolar diameter change. Our findings may indicate a contribution of macro-microvascular crosstalk in diabetes complication development.

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ASSOCIATION BETWEEN AMBULATORY ARTERIAL STIFFNESS INDEX, MARKERS OF BLOOD PRESSURE VARIABILITY AND INDICES OF SUBCLINICAL VASCULAR DAMAGE IN OBESE CHILDREN

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Objective: Ambulatory Arterial Stiffness Index (AASI) and symmetric AASI (sAASI) have been proposed as indices of arterial stiffness obtained by 24-hour ambulatory blood pressure monitoring (ABPM). ABPM allows the analysis of indices of BP variability like day and night SD, BP dipping, weighted 24-h SD (wSD), average real variability (ARV). Aim of the present study was to address the relationship between these indices and other markers of vascular subclinical damage in children.

Design and Method: 45 obese children were included. Children underwent vascular measurements, including: (i) office and 24-hour ambulatory BP; (ii) brachial flow-mediated dilatation (FMD), carotid intima media thickness (cIMT), and distensibility (cDC); (iii) systemic arterial stiffness (SIDVP). From ABPM we calculate AASI, sAASI, ARV, SD, SD, systolic and diastolic dipping and wSD.

Results: ARV showed a significant correlation with SIDVP (r = 0.379; p = 0.023). AASI but not sAASI correlated with FMD (r = 0.361; p = 0.031). In the population divided in hypertensive (n = 11)/normotensive (n = 34), ARV was associated with SIDVP only in normotensive (r = 0.446; p = 0.015). In normotensive, z score-BMI was correlated with both sAASI and wSD (respectively 0.340; p = 0.049 and 0.423; p = 0.014), wSD correlated with FMD (r = 0.384; p = 0.048); in hypertensive children, ARV