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P152: MICROALBUMINURIA IN NEWLY DIAGNOSED DIABETES MELLITUS: NOT ONLY ABOUT BLOOD PRESSURE OR ARTERIAL STIFFNESS

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Japan (cardio-ankle vascular index) method. Blood samples were taken for ELISA assays. Analysis was completed with SPSS software

Results: Forty patients were evaluated in this preliminary project (29 male/11 female, mean age 70.7 ± 11.99), with four experiencing a further event during the six month follow up (10%).

All biomarkers and both measurements for arterial stiffness had a higher mean value in patients with a further event (hsCRP 3.89 vs 1.42, $P = 0.08$; EPO 9.06 vs 9.01, $P = 0.85$; sRANKL 0.05 vs 0.03, $P = 0.31$; PRDX1 6.27 vs 6.21, $P = 0.95$; CAVI 11.13 vs 9.69, $P = 0.15$; cfPWV 10.82 vs 10.2, $P = 0.55$), however none were statistically significant.

Levels of PRDX1 were elevated acutely post-event before falling significantly ($R = -0.475$, $P = 0.002$), while hsCRP and EPO continued to be elevated at >10 days post-event.

In addition, CAVI correlated closely with hsCRP ($R = 0.28$, $P = 0.09$) and EPO ($R = 0.29$, $P = 0.08$), but cfPWV was not closely related to any of the biomarkers.

Conclusions: This preliminary data suggests that biomarkers, particularly EPO and hsCRP, are more closely related to CAVI than cfPWV. hsCRP was the most relevant as an independent predictive factor for further vascular events.

Poster Session II – Obesity and Diabetes

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ARTERIAL STIFFNESS AND PROGRESSION OF CEREBRAL WHITE MATTER LESIONS IN ASYMPTOMATIC PATIENTS WITH TYPE 2 DIABETES AND MATCHED CONTROLS: A 5-YEAR COHORT STUDY

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Aim: Stroke is a frequent and feared complication in patients with type 2 diabetes. Arterial stiffness may improve current suboptimal risk prediction of stroke. However, studies in diabetes populations are lacking. We investigated the association between arterial stiffness progression (carotid-femoral pulse wave velocity [PWV]) and the progression of cerebral white matter lesions (WML), a marker of stroke risk, in patients with type 2 diabetes and matched controls.

Methods: In a 5-year follow-up study, data from 49 patients and 58 controls were available for analysis. At baseline, participants had a mean (\pm SD) age of 59 ± 10 years and patients had a median (range) diabetes duration of 1.8 (1.0–3.2) years. Fifty-two (49%) were males. At both baseline and follow-up, PWV was obtained by tonometry and WML by cerebral T2-FLAIR MRI. WML was assessed by Breteler score, and progression was defined as an upward change in category during follow-up.

Results: Patients with type 2 diabetes had a higher PWV than controls at both baseline (9.2 ± 2.2 vs. 7.9 ± 1.4 m/s, $p < 0.01$) and follow-up (9.8 ± 2.4 vs. 8.6 ± 1.9 m/s, $p = 0.01$). Breteler scores and WML progression were similar in the two groups ($p > 0.05$). PWV progression was associated with WML progression in the total cohort (adjusted for age, sex, diabetes, baseline PWV and systolic blood pressure progression: OR 1.58 [95%CI: 1.09–2.28], $p = 0.02$). We found no interaction between diabetes and PWV progression on WML progression.

Conclusions: PWV progression is associated with WML progression in patients with type 2 diabetes and healthy controls. PWV candidates as a new risk marker for stroke.

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CENTRAL PULSE PRESSURE IS ASSOCIATED WITH AORTIC-BRACHIAL STIFFNESS MISMATCH IN PATIENTS WITH ARTERIAL HYPERTENSION AND DIABETES MELLITUS

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Background: Central pulse pressure (PP) is a surrogate measure of arterial stiffness (AS) and a predictor of cardiovascular events in type 2 diabetes mellitus (T2DM). AS gradient reflects the vascular ageing.

The aim of the study: To evaluate the associations between 24-h central PP and parameters of AS in patients with arterial hypertension (AH) and T2DM. **Materials and methods:** 90 patients with AH and T2DM were included (39% males, mean age 63.8 ± 11.6). Mean office BP was $146 \pm 23/86 \pm 10$ mmHg. Median duration of DM was 8.5 years. 24-h peripheral and central BP monitoring was performed (BPLab Vasotens). AS parameters were assessed by applanation tonometry (Sphygmocor, AtCor). AS gradient was calculated as cfPWV/crPWV and its elevation ≥ 1 was considered as AS mismatch. $p < 0.05$ was considered significant.

Results: Mean central BP was $132 \pm 18/79 \pm 12$ mmHg, cfPWV -10.5 ± 2.4 m/s, crPWV -8.5 ± 1.4 m/s, AS gradient -1.2 ± 0.3 . 24-h central BP levels were as follows: $132 \pm 18/79 \pm 12$ mmHg for 24hBP, $132 \pm 18/81 \pm 13$ mmHg for daytime and $129 \pm 20/75 \pm 11$ mmHg for nighttime. Mean PP levels were 53 ± 14 , 52 ± 14 and 56 ± 15 mmHg, respectively. 24-h central PP increase > 50 mmHg was observed in 30% patients. These patients were older (67.1 ± 10.5 vs 61.8 ± 11.9 years), had higher median duration of DM (10; IQR 7–15 vs 5; IQR 0, 9–12 years), cfPWV (11.4 ± 1.9 vs 10.0 ± 2.6 m/s) and stiffness gradient (1.4 ± 0.3 vs 1.2 ± 0.2), $p < 0.05$ for trend. There were significant correlations between 24-h central PP and age ($r = 0.27$) and AS gradient ($r = 0.32$), $p < 0.05$ for trend. No predictors of PP elevation were found.

Conclusions: In diabetic patients with AH increase of central PP is associated with aortic-brachial stiffness mismatch. This finding confirms its importance as a marker of vascular ageing in this patient population.

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MICROALBUMINURIA IN NEWLY DIAGNOSED DIABETES MELLITUS: NOT ONLY ABOUT BLOOD PRESSURE OR ARTERIAL STIFFNESS

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Background: Diabetes mellitus (DM) and hypertension (EH) are both associated with micro- and macro-vascular damage. Microalbuminuria is a recognized marker of sub-clinical target organ damage in both DM and EH. However, it's determinants in newly diagnosed DM with or without EH remain unclear.

Methods: We enrolled consecutive newly diagnosed DM patients, recording history, demographics, renal, lipid and glycemic profile, office and ambulatory blood pressure, macro-(pulse-wave velocity/PWV) and micro-vascular (microalbuminuria in 24-hour urine) damage and subclinical atherosclerosis (intima-media thickness).

Results: We studied 65 DM patients (40 male: 25 female, aged 57 ± 11 years), with a median duration from diagnosis of 2 weeks. Their fasting glucose was 121.5 (IR: 36) mg/dl, HbA1c: 7.47 (IR: 2%). Among them, 26 had already been diagnosed with EH (median duration of 8 (IR: 8) years), while 17 were diagnosed with EH at the time of DM diagnosis. No difference was observed between the two groups, except for significantly higher office and ambulatory BP and PWV in the newly diagnosed EH patients. Microalbuminuria was associated with fasting glucose ($p = 0.04$), HbA1c ($p = 0.002$), serum creatinine ($p = 0.035$), glomerular filtration rate (GFR) ($p = 0.002$), office systolic ($p = 0.009$) and diastolic ($p = 0.026$) BP and PWV ($p = 0.031$). In the multivariate analysis, HbA1c (beta = 0.351, $p = 0.015$) was the only determinant of microalbuminuria.

Conclusions: Our study indicates that hyperglycaemia has a significant impact on microalbuminuria even in patients with newly diagnosed DM and

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.