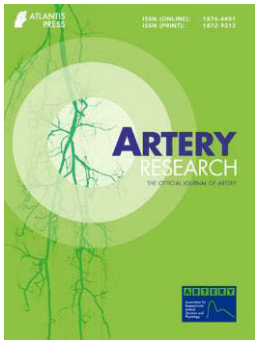

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# P144: IMPACT OF ANTI-HYPERTENSIVE DRUGS ON AORTIC STIFFNESS INDUCED BY CHRONIC KIDNEY DISEASE AND MINERAL BONE DISORDER IN RATS

Mohsen Agharazii, Roth-Visal Ung, Sarah-Kim Bisson, Fabrice Mac-Way, Darren E. Richard, Richard Larivière

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| | Non-T2DM-subjects (n=54) | Patients with T2DM (n= 111) | Unadjusted p-value | Age-gender-adjusted p-value | Adjusted p-value (potential confounders) |
|---|---|---|---|---|---|
| **Retinal parameters** | | | | | |
| ICD (μm) | 20.8 ± 3.5 | 23.9 ± 5.1 | <0.001 | <0.001 | 0.001 |
| RCF (AU) | 310.4 ± 55.1 | 297.8 ± 72.9 | 0.15 | 0.35 | 0.72 |
| WLR (-) | 0.35 ± 0.08 | 0.38 ± 0.11 | 0.04 | 0.67 | 0.90 |
| ***Renal parameters*** | | | | | |
| eGFR (ml/min/1.73m²) | 95.9 ± 17.3 | 91.7 ± 9.9 | 0.10 | <0.001 | <0.001 |
| UACR (mg/g) | 7.9 ± 7.5 | 21.3 ± 86.6 | <0.001 | 0.55 | 0.91 |
| **Vascular stiffness parameters of large arteries** | | | | | |
| cSBP (mmHg) | 106.7 ± 12.4 | 119.5 ± 12.9 | <0.001 | 0.37 | 0.81 |
| cPP (mmHg) | 34.8 ± 10.6 | 41.8 ± 11.7 | 0.001 | 0.31 | <0.001 |

**P143**

**REDUCED LEVELS OF ANTI-AGEING HORMONE KLOTHO ARE ASSOCIATED WITH INCREASED AORTIC STIFFNESS IN PATIENTS WITH TYPE 2 DIABETES**

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**Background:** Aortic Pulse Wave Velocity (Ao-PWV) predicts cardiovascular disease and renal dysfunction in Type 2 Diabetes (T2DM). Klotho is a circulating anti-ageing hormone that has direct cardio-renal protective effects in animal studies. We have previously demonstrated that circulating levels of Klotho are increased by Renin-angiotensin System inhibition (RASi), inversely associated with albuminuria and predict renal function decline in T2DM. The relationship between Klotho and Ao-PWV in diabetes is unknown.
**Methods:** We investigated the correlation of serum Klotho levels and Ao-PWV in 92 patients with T2DM (61% male) all on RASi with preserved renal function in a cross-sectional study. Klotho levels were measured using a validated immunoassay and Ao-PWV by applanation tonometry (Sphygmocor system).
**Results:** The mean age (range) of our cohort was 60.4 (40—82) years with an estimated GFR (using CKD-EPI equation) of 89.2 (46—143) ml/min. Median (interquartile range) Ao-PWV and circulating Klotho levels were 11.8 (10.3—13.6) m/s and 201.46 (154.64—280.17) pg/μl respectively. Patients with an Ao-PWV above the median were older (62.8 ± 9.9 vs 58.1 ± 8.2 years), had a higher SBP (160.9 ± 10.01 vs. 155.04 ± 11.7 mmHg) and lower Klotho levels (192.59 [120.27—255.45] pg/μl vs 219.92 [171.06—311.56] pg/μl), compared to those below the median (p = 0.05 for all).A 10% increase in circulating Klotho levels significantly reduced the odds of a patient being above the Ao-PWV median by 11% in a multivariable logistic regression analysis.
**Conclusion:** There is an inverse association between Ao-PWV and circulating Klotho levels in T2DM. Treatments and strategies that that increase Klotho may attenuate aortic stiffness in diabetes.

**P144**

**IMPACT OF ANTI-HYPERTENSIVE DRUGS ON AORTIC STIFFNESS INDUCED BY CHRONIC KIDNEY DISEASE AND MINERAL BONE DISORDER IN RATS**

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**Background:** In chronic kidney disease (CKD), anomalies of mineral bone disorder (MBD) play a central role in vascular calcification and increased aortic stiffness. The impact of antihypertensive drugs on MBD-induced vascular calcification remains uncertain. The aim of this study was to examine whether endothelin A receptor antagonist (ETAA), angiotensin type-1 receptor antagonist (AT1A) and the combination of hydralazine/hydrochlorothiazide (HDZ/HCT) can reduce vascular stiffness in a rat model of CKD-MBD.
**Method:** Using a remnant kidney model of CKD in rats, vascular calcification was induced by creating MBD through high a calcium-phosphate diet and vitamin D supplementation. Three antihypertensive treatments were investigated: atrasentan (ETA blocker), losartan (AT1 blocker) and HDZ/HCT. Blood pressures (BPs) were measured invasively after (6 weeks) and aortic stiffness was determined by the assessment of pulse wave velocity (PWV).
**Results:** PWV and mean BP increased in rats with CKD-MBD as compared to CKD (640 ± 130 vs. 390 ± 34 cm/s and 100 ± 17 vs. 92 ± 21 mmHg; p p < 0.05). Treatment of CKD-MBD rats with $ETA_A$ and $AT1_A$, but not HDZ/HCT, reduced PWV (517 ± 94, 596 ± 134 and 761 ± 116 cm/s respectively) despite similar reduction of mean BP by the different treatments (73 ± 16, 75 ± 19 and 70 ± 20 mmHg, respectively). Creatinine clearance and mineral metabolism parameters were relatively similar among groups.
**Conclusion:** MBD-induced aortic stiffness in CKD rats was improved by atrasentan and losartan, but not the combination of HDZ/HCT, indicating blood pressure-independent protective effects of $ETA_A$ and $AT1_A$.

**P145**

**ARTERIAL STIFFNESS AND LEFT VENTRICULAR DIASTOLIC FUNCTION IN PATIENTS WITH METABOLIC SYNDROME: LONGITUDINAL STUDY**

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**Aim:** To evaluate the relation between arterial stiffness and left ventricular diastolic dysfunction (LVDD) in metabolic syndrome (MetS) patients during more than 3 years observation period (average was 3,8 years).
**Methods:** This longitudinal study enrolled 573 subjects (aged 53,4 ± 6 years, 63% female, 76% hypertensive) from the Lithuanian High Cardiovascular Risk Primary Prevention Programme1, without overt atherosclerotic disease and systolic LV dysfunction. Arterial stiffness parameters (carotid-to-femoral pulse wave velocity(cfPWV), augmentation index (AIxHR75), mean aortic pressure(mAP), central pulse pressure(cPP) were assessed by applanation tonometry. Diastolic function (LVDF) was defined according to the 2016 ESC Guidelines for diagnosis and treatment of acute and chronic heart failure.
**Results:** In presented cohort most of study subjects had LVDD at first visit (n = 418, n = 325 impaired relaxation, n = 92 pseudonormalisation, n = 1 restrictive LVDD). During the observation LVDF didn't change in 337 (GR1), deteriorated in 110 (GR2), improved in 126 (GR0) participants. We found significant alterations of arterial and diastolic function parameters(mean): cfPWV 8,55 ± 1,4 vs 8,7 ± 1,6 m/s; AIxHR75 22,8 ± 10,4 vs 24,3 ± 10,8%; mAP 105,3 ± 10,4 vs 101,5±14,8 mmHg; cPP 42,6 ± 9,9 vs 43,3 ± 10,6 mmHg; E/A ratio 1 ± 0,3 vs 0,93 ± 0,2; E/e'mean ratio 10,4 ± 3,5 vs 9,4 ± 2,9; E/e'septal 11,9 ± 4,1 vs 10,9 ± 3,2; MMI 105 ± 22,7 vs 99 ± 24,1 (p < 0,05 for all). Significant correlations were found between initial arterial indices and alterations of LVDF: in GR1 with E/Aratio (rcfPWV = −0.176); in GR0 with E/e'mean