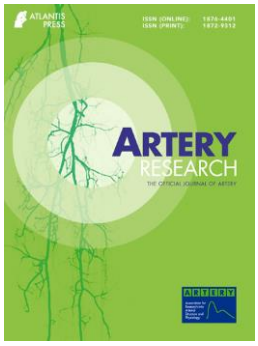

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P4.26: ASSOCIATIONS BETWEEN FGF23-LEVEL AND ARTERIAL DISTENSIBILITY IN CHRONIC KIDNEY DISEASE

O. Cseprekal, Németh Zs, A. Marton, E. Vámos, J. Nemcsik, J. Egresits, T. El Hajd Othmane, B. Fekete, Deák Gy, I. Kiss, A. Tislér

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4.6±1.5 ng/ml; P<0.01) and higher PWV (9.5±1.4 vs 8.4±1.3 m/s; P<0.001). Kaplan–Meier survival curves for MACE by TT tertiles at baseline are shown in figure. Subjects in the lowest TT tertile (<4.0 ng/ml) had a statistically significant higher risk of MACE compared to those in the highest tertile (>4.9 ng/ml) in multivariate Cox models adjusted for age, systolic blood pressure and risk factors (all P<0.05). Addition of TT to standard risk factors model yielded a net reclassification improvement of 38.8% (P<0.05). In regression analysis, PWV was inversely associated with TT (β=-0.207, P<0.001), indicating deterioration of aortic stiffness with decreasing testosterone level.

Conclusions: The principal finding of our study is that androgen deficiency predicts independently MACE in long-term follow-up in hypertensive patients. The association of TT with aortic stiffness may suggest other mechanisms, such as changes in vascular function and structure.

P4.23
CORRECTION OF VITAMIN D DEFICIENCY BY CALCIFEDIOL IN HYPERTENSIVES WITH STAGE 3 CHRONIC KIDNEY DISEASE REDUCES PULSE WAVE VELOCITY BY LOWERING BLOOD PRESSURE

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Objectives: To measure the extent of correction of vitamin D deficiency and hyperparathyroidism after treatment with calcifediol as well as their relationship to blood pressure and arterial stiffness in hypertensive patients with stage 3 chronic kidney disease (CKD).
Methods: Longitudinal study that included 74 treated hypertensives (46 women, 62,2%) with stage 3 CKD (eGFR 47,7 ml/min, SD±10) without previous vitamin D supplementation treatment. Calcifediol 266 μg/2 weeks and calcium 600 mg/d were given if baseline-vitamin D < 30 ng/ml and < 9,5 mmol/l, respectively. A second visit took place after 4 months.
Results: The mean age was 72,9 years (SD±10). The prevalence of vitamin D deficiency decreased from initially 96% to 23% (mean baseline: 18, mean final: 42 ng/ml), and of secondary hyperparathytoidism from 62% to 37% (mean at baseline: 87, mean final: 63 pg/ml). There were no significant changes in eGFR, calcium or phosphor or number of antihypertensive drugs, but pulse wave velocity (measured with MOBILOGRAPH®) and BP decreased significantly form initially 133/76 to 123/72 (p<0.001) mmHg and from 10,8 to 10,5 m/sec (p<0.005), respectively. In bivariate analysis the difference between baseline and final vitamin D and PTH correlated significantly. The only variable significantly related to the change in PWV was the difference in peripheral SBP. Only one case of asymptomatic hypercalcemia was observed.
Conclusions: In hypertensive patients with stage 3 CKD, correction of vitamin D deficiency by oral caldifediol leads to a substantial reduction of incipient hyperparathyroidism and a significant decrease of arterial stiffness.

P4.24
DIETARY INORGANIC NITRATE LOWERS CENTRAL BLOOD PRESSURE

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Background: Dietary inorganic nitrate is reduced to (nitric oxide) NO in the body. Beetroot is a rich source of dietary inorganic nitrate and has been shown to lower brachial blood pressure (BP) by this mechanism. The effect on aortic (central) BP, which may be a better predictor of cardiovascular disease, has not been studied.
Objectives: To measure the effect of dietary nitrate in beetroot juice on central BP at both 30 minutes and over a 6 hour period post-beetroot juice consumption.
Method: A double-blind, randomised, placebo-controlled crossover trial was performed in nine healthy, normotensive men and women aged between 22 and 45 years. Participants were randomised to receive beetroot juice (6.5-7.3 mmol nitrate) or placebo juice (0.04-0.06 mmol nitrate). Brachial and central BP were measured at baseline, 30 and 60 minutes post-ingestion, and at least hourly for the following 24 hours. Following a washout period, the procedure was repeated within seven days with crossover to the opposite arm of the trial. There were no dietary restrictions during the study.
Results: Compared with placebo, beetroot juice lowered central systolic BP at 30 minutes (change in beetroot juice: -2.6±3.4 mmHg vs. change in placebo: 1.8±5.9 mmHg, $P=0.045$). Beetroot juice also lowered central systolic BP averaged over 6 hours post-ingestion (beetroot: 106±8 mmHg vs. placebo: 111±11 mmHg, $P=0.029$).
Conclusion: Consumption of beetroot juice lowered central BP. Beetroot juice could have a role in CV risk management in the general population, but further research is required to establish its long-term benefits, safety and tolerability.

P4.25
COMPARISON BETWEEN EFFECTS OF BEZAFIBRATE AND EICOSAPENTAENOIC ACID ON ARTERIAL STIFFNESS MONITORING WITH CARDIO-ANKLE VASCULAR INDEX

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Background: Bezafibrate and Eicosapentanoic acid (EPA) were known to decrease serum triglyceride. And, EPA administration for 5 years was reported to improve cardiovascular events by JLIT study. Cardio-ankle vascular index (CAVI) was a new index reflecting arterial stiffness from the origin of the aorta to the ankle, and is reported to be a predictor of cardiac events or death rate of cardiovascular events. But, the effects of both agents on arterial stiffness were not fully clarified.
Object: The purpose of this paper is to clarify the effect of bezafibrate and EPA on the arterial stiffness monitored with CAVI in the type 2 diabetic patients with hypertriglyceridemia.
Subjects and methods: Eighty type 2 diabetic outpatients with hypertriglyceridemia were randomly divided into two groups: bezafibrate (BEZA; 400mg/day) and EPA (1800mg/day) groups and took each treatment for 6 months. Glucose and lipid metabolism, d-ROMs; an oxidative stress marker were also studied. CAVI was measured using Vasela1500 (Fukuda Denshi. Co.LTD).
Results: After 6 month treatment, blood pressure, LDL-cholesterol (LDL-C), CK were not significantly changed comparing with before values, in both groups. Triglyceride (TG) and remnant-like particle cholesterol decreased significantly in both groups, and there were no significant differences between groups. HDL-C, Apo A-1 increased and HbA1C, d-ROMs decreased significantly only in BEZA group. CAVI decreased by 0.1 in EPA group (not significant) and by 0.5 in BEZA group (p<0.005). There was a significant difference in the changes of CAVI between both groups (p<0.05). In BEZA group, there were no significant correlations between changes of CAVI and the changes of the other parameters.
Conclusion: Bezafibrate administration improved arterial stiffness monitored with CAVI significantly, whereas EPA administration did not changed CAVI, in type 2 diabetic patients with hypertriglyceridemia.

P4.26
ASSOCIATIONS BETWEEN FGF23-LEVEL AND ARTERIAL DISTENSIBILITY IN CHRONIC KIDNEY DISEASE

O. Cseprekal [1], Németh Zs [3], A. Marton [3], E. Vámos [1], J. Nemcsik [4], J. Egresits [1], T. El Hajd Othmane [1], B. Fekete [1], Deák Gy [3], I. Kiss [2], A. Tislér [1]
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Vascular calcification and hemodynamical abnormalities lead to reduced arterial elasticity in end stage renal disease. Fibroblast growth factor-23 (FGF23) predicts cardiovascular mortality in advance stages of renal failure possibly indicating more advanced vascular calcification. The relation of FGF23 to arterial stiffness in chronic kidney disease is currently under investigations.
The aim of our cross sectional study was to assess the potential associations between FGF23 and arterial distensibility.
FGF23 (ELISA), pulse wave velocity (PWV), augmentation index (AI) and central pulse pressure (CPP) (PulsePen), were measured in patients with

different stages of renal insufficiency (n=103, 64.8±13.3 years, 50 males, eGFR 40±21 mL/min/1.73m^2). Univariate and multiple linear regression models were used for the statistical analysis.
According to our results, logFGF23 showed significant relation with serum phosphate, PTH levels and renal function. There were no significant correlations between FGF23 and PWV or CPP. AI, however, correlated negatively with logFGF23 (r= -0.24, p<0.05). By multiple regressions, serum phosphate, logFGF23, systolic blood pressure and heart rate proved to be the individual predictors of AI. (R^2=0.31, ß=0.31, -0.33, 0.21, -0.27, p<0.05). In the subgroup of patients with <45 mL/min/1.73m^2 eGFR, serum phosphate and logFGF23 remained the significant predictors (R^2 0.21, ß=0.31, -0.39, p<0.05)
FGF23 may be a determinant of peripheral arterial elasticity independently of serum phosphate level especially in advanced stages of chronic kidney disease.
(Supported by the Hungarian Kidney Foundation and the Hungarian Society of Hypertension)

P4.27
DIABETES-EVOKED PATHOGENIC CHANGES ASSOCIATED WITH ALTERED COPPER UPTAKE/TRANSPORT PATHWAYS IN THE AORTA OF STZ-DIABETIC RATS: EFFECTS OF TREATMENT BY CU(II)-SELECTIVE CHELATION

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Objectives: Cardiovascular disease is the commonest complication of diabetes. Previous studies from our group have identified diabetes-evoked changes in copper homeostasis that cause accumulation of chelatable-Cu(II) in the heart (1). We also showed that treatment by Cu(II)-selective chelation with TETA (triethylenetetramine) ameliorates cardiac left-ventricular/aortic damage in diabetes (2). This study aimed to define the pathogenic role of copper imbalance in diabetic arteriopathy and its response to TETA.
Methods: Pathological changes in the aorta of STZ-diabetic rats with/without TETA treatment were examined by histological and confocal imaging. Expression of genes and proteins involved in regulation of copper uptake/transport in aortic tissues were analysed by RT-qPCR and Western blotting.
Results: Diabetes-induced oxidative aortic damage was associated with increased expression of ET-1, ET-A, ICAM1 and eNOS, and decreased expression of Ctr1 (cell-membrane copper-uptake transporter-1) and Sco1 (copper-chaperone 1 for cytochrome c oxidase). We also identified up-regulation of CCS (copper chaperone for SOD1) and copper-binding metallothioneins (MT1/2) as further compensatory responses apparently aimed at up-regulating copper-related defences in response to altered aortic copper regulation in diabetes. TETA treatment further elevated MT1/2 levels. Moreover, diabetes lowered levels/activity of SOD2, both of which were restored by TETA treatment.
Conclusions: Dysregulation of cellular copper uptake/transport might be an important molecular process contributing to the pathogenesis of diabetic arteriopathy, and TETA treatment could be beneficial by restoring of these acquired defects, at least in part via activation of MT1/2 which are potent antioxidants, and SOD2, the main antioxidant enzyme that scavenges intra-mitochondrial superoxide radical.
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P4.28
GLYCAEMIC HOMEOSTASIS, ARTERIAL STIFFNESS AND DIASTOLIC FUNCTION IN HEALTHY SUBJECTS

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Objectives: To examine the impact of glycaemic homeostasis on arterial stiffness and cardiac diastolic function in healthy subjects.
Methods: Subjects (100 male & 115 female) were normotensive and normolipidaemic and had normal oral glucose tolerance test responses. Carotid-femoral arterial stiffness (PWV) and atherosclerotic risk (carotid intima media thickness; CIMT) were measured. Early/late mitral valve filling velocity (MV E/A) and isovolumetric relaxation time (IVRT) was used to assess diastolic function. Glycosylated haemoglobin (HbA_{1c}) was used to determine long-term glycaemic homeostasis. Anthropometrical measurements such as height, body mass and waist circumference were also measured.
Results: Spearman's correlation identified significant association between HbA_{1c} and age (r=0.40, P<0.0001), waist height ratio (r=0.18, P<0.01), PWV (r=0.26, P<0.001), CIMT (r=0.18, P<0.05), MV E/A (r=-0.37, P<0.0001) and IVRT (r=0.28, P<0.01). In multiple regression analysis's age remained the only independent predictor of PWV, CIMT, MV E/A and IVRT.
Conclusion: Despite being clinically healthy, HbA_{1c} is associated with greater arterial stiffness and poor diastolic function.

P4.29
COMPARATIVE EFFECTS OF ANTIHYPERTENSIVE DRUGS ON OXIDATIVE STRESS AND INFLAMMATION

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Objective: Oxidative stress and vascular inflammation are increased in hypertension. These factors may contribute to target organ damage and increased cardiovascular risk in these patients. We studied the effect of four classes of antihypertensive drugs on oxidative stress and inflammatory markers in patients with essential hypertension.
Design and method: In this double-blind placebo-controlled crossover study we randomized 41 treatment-naïve hypertensive patients to receive doxazosin 4 mg, candesartan 16 mg , bisoprolol 5 mg, isosorbide mononitrate 50 mg, and placebo daily for 6 weeks. Brachial blood pressure (BP), plasma high sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), asymmetric dimethylarginine (ADMA), oxidized LDL (oxLDL), soluble intercellular adhesion molecule-1 (sICAM-1), oxLDL antibodies (OLAB), and urine 8-isoprostanes were measured after each treatment period.
Results: All drugs reduced systolic, diastolic, and mean arterial pressure (p<0.001) with candesartan having the greatest effect. None of the drugs reduced inflammatory or oxidative stress markers compared to placebo. There were significant differences in between-drug analysis. Doxazosin reduced OLAB and oxLDL levels the most (p<0.05). With bisoprolol there was a trend for hsCRP and ADMA level increase compared to other drugs (p<0.01). There were no differences regarding drug effects on sICAM-1, IL-6, or 8-isoprostane levels. Changes in oxLDL and to lesser degree hsCRP and sICAM-1 levels correlated with change in BP with study drugs.
Conclusions: In our study an alpha-blocker seemed to have the most favorable effect on oxidative stress and inflammatory markers while a beta-blocker had least effect. These effects are partially dependent on the BP-lowering effects of the drugs.

P4.30
ENDOTHELIAL DYSFUNCTION AND CARDIOVASCULAR RISK PROFILE IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION

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Background/aims: The impact of chronic hepatitis C (HCV) virus infection on atherosclerosis is controversial. In this pilot clinical study, we examined whether HCV patients significantly differed in markers of subclinical atherosclerosis compared to patients with alcohol-related chronic liver disease.
Methods: We enrolled 21 consecutive adult patients with HCV and 11 patients with alcohol-related chronic liver disease after detoxification from alcohol. Common carotid intima-media thickness (CIMT) and brachial artery flow mediated vasodilation (FMD) by ultrasonography and carotid-femoral