ORAL SESSION

ORAL SESSION 4A:
KIDNEY

URINARY UROMODULIN IN A PATHWAY BETWEEN DECREASED URINARY URIC ACID EXCRETION AND ALBUMINURIA

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Objective: The mechanism explaining the inverse relationship between urinary uric acid and albumin excretion remains unclear. First, we evaluated the impact of candidate SNPs in the urate transporter SLC2A9 gene on the relationship between fractional excretion of uric acid (FEUA) and urinary albumin/creatinine ratio (uACR). Second, we examined urinary uromodulin and sodium excretion as mediators of the relationship between FEUA and uACR.

Design and method: We analyzed 737 French Canadians from the CARTaGENE cohort, a random sample of the Quebec population aged 40–69 years of 20,004 individuals. French Canadians with available genotyping and urinary data were obtained from a sub-study examining associations between common variants and cardiovascular disease in gender-matched individuals with high and low Framingham Risk Score and vascular rigidity index. We further excluded individuals with an eGFR < 60 ml/min/1.73m2, glycosuria, and use of confounding medication. A spot urine sample was analyzed. Genotyping was performed using the Illumina HumanOmni2.5–8 BeadChips. Two SNPs (rs16890979; rs13129697) were analyzed using an additive model.

Results: Final analyses included 593 individuals (45.5% of men; mean age 54.3 ± 8.6). The rs13129697 G homozygotes within the 1st and 2nd FEUA tertiles had higher estimated mean of uACR compared to those within the 3rd tertile ($p = 0.001$; $p = 0.006$, respectively), as well as compared to heterozygotes ($p = 0.006$; $p = 0.005$, respectively) and T homozygotes ($p = 0.004$; $p = 0.001$, respectively). Contrarily, no difference in uACR by FEUA tertiles was observed in T homozygotes and heterozygotes. In a reference regression model for uACR, an increase in mean blood pressure and plasma glucose, a decrease in FEUA, and female gender were associated with an increase in uACR, whereas carriage of each copy of the rs13129697 T allele was associated with a decrease in uACR. Using the mediation analysis, uromodulin explained 32%, fractional excretion of sodium (FENa) 44%, and uromodulin together with FENa explained 70% of the relationship between FEUA and uACR. Bootstrapping process confirmed the role of both mediators.

Conclusions: Our data suggest that the relationship of albuminuria with decreased urate excretion may be facilitated by the urate transporter SLC2A9, and mediated by urinary uromodulin, possibly through its effect on sodium reabsorption.

EVALUATION OF INTRA-RENAL BLOOD FLOW PARAMETERS IN PATIENTS WITH RENAL FIBROMUSCULAR DYSPLASIA - THE POLISH REGISTRY FOR FIBROMUSCULAR DYSPLASIA (ARCADIA-POL STUDY)

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Objective: To assess intra-renal blood flow parameters in patients with renal fibromuscular dysplasia (FMD) in patients with renal FMD enrolled to ARCADIA-POL study.

Design and method: We analyzed 143 patients with renal FMD enrolled in the ARCADIA-POL study since 2015 (Polish-French collaboration). All patients underwent evaluation including ABPM, biochemical evaluation, biobanking, duplex Doppler of carotid and abdominal arteries and whole body angio-CT. We divided patients with renal FMD into two groups – 31 patients with significant renal artery stenosis (RAS) (26F, 5 M, mean age:19.8 ± 12.7 years) and 112 patients with non-significant RAS (93 F, 19 M, mean age:47.2 ± 14.9 years). We compared those two groups to the matched control groups – 60 normotensive individuals (44F, 16 M, mean age:42.5 ± 9.1 years) and 60 patients with primary hypertension(40F, 20 M), mean age: 43.3 ± 11.4 years.

Results: FMD patients with non-significant RAS, FMD patients with significant RAS, normotensives and patients with primary hypertension differed significantly in resistive indexes values (RI) (0.59 ± 0.08 vs 0.53 ± 0.09 vs 0.61 ± 0.06 vs 0.62 ± 0.06, respectively $p < 0.001$; FMD patients with significant RAS vs normotensives: $p < 0.001$; vs patients primary hypertension: $p < 0.001$). In patients with FMD with significant RAS there was a significant correlation between RI and IMT ($r = –0.658$; $p = 0.008$). Subsequently we performed analysis "per kidney" and we compared three groups of renal arteries in FMD patients-renal arteries with no FMD lesions (n = 75), renal arteries with FMD with non-significant RAS (n = 180) and renal arteries with FMD with significant RAS (n = 31). FMD renal arteries with significant RAS were characterized by lower RI value, higher maximal blood flow velocity (Vmax), higher renal aortic ratio (RAR) and higher acceleration time (AT) as compared to both FMD renal arteries with non-significant RAS and renal arteries with no FMD lesions. No differences in intra-renal blood flow parameters were found between FMD renal arteries with non-significant RAS and renal arteries with no FMD lesions.

Conclusions: Our results indicate that FMD patients with significant RAS are characterized by changes in intra-renal blood flow parameters as those observed in atherosclerotic RAS. Moreover those changes were related to carotid arteries IMT.

HYPERTENSION IN ADOLESCENCE INCREASES THE RISK FOR FUTURE END-STAGE RENAL DISEASE: A NATIONWIDE COHORT OF 2.65 MILLION ADOLESCENTS

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Objective: Hypertension among adolescents is an emerging public health issue. The association of adult hypertension (HTN) with end-stage renal disease (ESRD) is well established. In contrary, because of scarce data, the role of HTN in otherwise healthy adolescents as an initiating factor leading to future ESRD is unclear. The aim of this study was to investigate the association between HTN and ESRD in otherwise healthy adolescents and among non-overweight adolescents in particular.

Design and method: Socio-demographic and medical data of 16–19 years old military conscripts who underwent comprehensive medical assessment prior to their military service during the years 1967–2013 were linked with the Israeli registry of ESRD to create a nationwide large population-based retrospective cohort. Cox proportional hazard models were used to estimate the association of well-established adolescence HTN and future ESRD among the general cohort population and among non-overweight in particular.

Results: The cohort included 2,658,238 adolescent conscripts of whom 7997 (0.3%) had HTN. Half of the hypertensive adolescents were overweight, and 90% were males. During a follow-up of 45,700,336 person-years, 2189 subjects developed ESRD with an incidence rate of 4.8 per 100,000 person-years. Adolescence

HTN was associated with future ESRD with a crude hazard ratio (HR) of 5.068 (95% CI, 3.734–6.879). In multivariate model adjusted for sex, age, year, weight and other socio-demographic variables, the HR was 1.980 (95% CI, 1.417–2.768). In further analysis excluding adolescents with severe HTN the association with ESRD remained significant (HR 1.925, 95% CI, 1.371–2.702). In sub analysis of the non-overweight adolescents the association between HTN and ESRD was significant as well (HR 2.114, 95% CI, 1.053–4.244).

Conclusions: Adolescence HTN doubled the risk for future ESRD regardless to overweight and to the severity of the hypertension.

CYSTATIN C AS A PREDICTOR OF MORTALITY AND CARDIOVASCULAR RISK IN A HYPERTENSIVE POPULATION

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Objective: Chronic kidney disease (CKD) is a predictor of all-cause mortality and cardiovascular events. Our aim was to determine whether cystatin C, a kidney function biomarker, can better predict both mortality and cardiovascular events than creatinine in hypertensive patients.

Design and method: We carried on a longitudinal, retrospective research with patients from a Hypertensive Unit. CKD was defined as serum creatinine levels greater than 1,1 mg/dl in men, and 0,8 mg/dl in women, and serum cystatin C levels greater than 1,1 mg/dl irrespective of gender. We chose two primary outcomes: all-cause mortality, and cardiovascular morbidity-mortality, i.e., non-fatal acute myocardial infarction, non-fatal stroke, heart failure and cardiovascular death.
We performed survival analyses using the Cox proportional hazard regression, including all potential predictors related to the primary outcomes. Hazard ratios (HR) were computed using R as statistical software.

Table 1. Clinical features of our cohort

	Men	Female	Total
Patients	737	734	1,471
Age (years)	55.9 (12.6)	60.3 (12.7)	58.1 (12.8)
BMI	30.1 (5.1)	30.8 (5.7)	30.5 (5.4)
Diabetes mellitus(%)	30.4	28.6)	29.5
Systolic BP (mmHg)	146.0 (17.7)	146.7 (19.8)	146.3 (18.8)
Diastolic BP (mmHg)	85.1 (11.2)	82.6 (11.2)	83.9 (11.2)
LDL-cholesterol (mg/dl)	131.2 (31.8)	137.8 (35.1)	134.5 (33.6)
HDL-cholesterol (mg/dl)	60.2 (16.6)	69.4 (17.9)	64.8 (17.8)
HbA1c (%)	6.0 (1.2)	6.0 (1.2)	6.0 (1.1)
Albumin/creatinine (mg/g)	18.9 (74.2)	22.0 (56.2)	20.9 (62.9)
Creatinine (mg/dl)	0.9 (0.2)	0.7 (0.2)	0.8 (0.2)
Cystatina C (mg/dl)	0.8 (0.3)	0.8 (0.3)	0.8 (0.3)
CKD-EPI-creat (ml/min/1.73m2)	93.2 (17.9)	90.8 (18.2)	92.0 (18.1)
CKD-EPI-cist (ml/min/1.73m2)	104.8 (26.7)	96.3 (25.1)	100.6 (26.2)
Presence of previous CV event (%)	16.3	10.6	13.5

Data are shown in percentage, for categorical variables, or median (interquartile rage) for continuous variables. CV: cardiovascular. BP: blood pressure. BMI: body mass index. HbA1c: glycated haemoglobin.

Table 2. Multivariate Cox proportional hazards regression model

	HR (CI 95%)	P-value
All-cause mortality		
CKD (creatinine)	1.2 (0.7 – 2.2)	0.4
CKD (cystatin C)	2.2 (1.15 – 4.1)	0.01
CV morbitidy-mortality		
CKD (creatinine)	1.3 (1.05 – 1.7)	0.01
CKD (cystatin C)	1.43 (1.04 – 1.9)	0.02

HR: hazard ratio. CKD: chronic kidney disease. Data was adjusted for age, gender, LDL- and HDL-cholesterol, systolic BP and HbA1c.

Results: We included 1,471 patients with a median age of 58 (table 1). Follow-up time was 11.7 years (median 4.8). We registered 103 myocardial infarctions, 145 strokes, 43 cases of heart failure, 39 cardiovascular deaths, and 19 non-cardiovascular deaths. Cystatin C turned out to have a better predictive value than creatinine, both for all-cause mortality (HR 2.2, 95% CI 1.15 – 4.1, p = 0.01) and cardiovascular morbidity-mortality (HR 1.43, 95% CI 1.04 – 1.9, p = 0.02), as shown in table 2.

Conclusions: In our hypertensive population cystatin, C proved to be a better predictor than creatinine, for both for all-cause mortality and cardiovascular morbidity-mortality. Our results suggest the determination of cystatin C can be useful when assessing cardiovascular risk in hypertensive patients.

LEVELS OF ENDOCAN, ANGIOPOIETIN-2 AND HIF-1A IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE AND DIFFERENT LEVELS OF RENAL FUNCTION

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Objective: Endothelial dysfunction leading to unbalanced vasoconstriction and ischemia of renal parenchyma is increasingly proposed as an additional pathway of renal damage in autosomal-dominant-polycystic-kidney-disease (ADPKD). However, human studies investigating the evolution of such phenomena are limited. This study investigated the levels of emerging biomarkers of endothelial function, angiogenesis and hypoxia, in ADPKD patients with different renal function.

Design and method: The study population consisted of three groups: 26 ADPKD patients with impaired renal function (Group A) (eGFR 45–70 ml/min/1.73m2), 26 ADPKD patients with preserved renal function (Group B) (eGFR > 70 ml/min/1.73m2), and 26 age- and sex- matched controls with no history of renal disease. Circulating levels of endocan (endothelial cell-specific molecule-1) angiopoietin-2, and hypoxia-induced-factor-1a (HIF-1a) were determined by ELISA techniques.

Results: Patients in Group A had significantly higher levels of endocan (7.17 ± 0.43 ng/ml), angiopoietin-2 (5,595.43 ± 3,390) and HIF-1a (163.68 ± 37.84 pg/ml) compared to patients in Group B (6.86 ± 0.59 ng/ml, p = 0.017, 3,854.41 ± 3,014.30, p = 0.018, 136.84 ± 42.10 pg/ml, p = 0.019, respectively) or controls (4.83 ± 0.69 ng/ml, 1,069 ± 427.88 pg/ml, 70.20 ± 17.49 pg/ml, p < 0.001 for all comparisons). Of note, patients in Group B had also higher levels of all markers compared to controls (p < 0.001), despite having similar renal function. In correlation analyses within ADPKD patients, we noted strong correlations of all studied markers with ADMA (endocan r = 0.908,p < 0.001, angiopoietin2 r = 0.983,p < 0.001 and HIF-1a r = 0.998,p < 0.001), and only weak or modest correlations with eGFR.

Conclusions: In conclusion, this study suggests that not only patients with low eGFR, but also those at early stages of the ADPKD had higher expression of markers indicative for endothelial dysfunction, angiogenesis and hypoxia in comparison to controls. These results could lead to the hypothesis that local microcirculatory changes may come early in the course of ADPKD and could be a cause rather than a result of disease progression and eGFR decline.

24HABPM IN THE LONG TERM FOLLOW UP OF RENAL TRANSPLANT PATIENTS: FOCUS ON AN UNMET CLINICAL NEED

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Objective: Non-dipping is much frequent in renal transplant patients and over 50% of these patients have nocturnal hypertension. Hypertension misclassification by office BP is quite common in this population and this phenomenon may alter therapeutic decisions in clinical practice. However, 24hABPM is not formally recommended by the current renal transplantation guidelines and it is rarely applied in most transplant centres.

Design and method: We performed a longitudinal study in 260 clinically stable renal transplant patients. All patients had at least one 24 h ABPM recording, 199 had two, 143 had three, 74 pts had four and 109 pts had > four ABPMs. Overall, 785 paired office and 24 h ABPM measurements over a 3.9 years median follow-up were available in the whole cohort. Data analysis was performed by the Generalized Estimating Equations (GEE) and the kappa statistics.

Results: At baseline visit on average both office (132 ± 16/78 ± 10 mmHg) and 24hABPM (125 ± 12/77 ± 9 mmHg) were controlled fairly well but as much as the 74% of patients had nocturnal hypertension by the ESH criterion (> = 120/70 mmHg). In an analysis by the General Estimating Equations, office BP (P = 0.97) and 24hABPM (P = 0.63) remained quite stable over follow up as it did the frequency of nocturnal hypertension (P = 0.64) which was 77% at the last observation. However, the global agreement of the two metrics for the classification of hypertension was very poor (k statistics 20%). In as much as 193 visits (25% of all

visits) where office BP indicated the need of antihypertensive therapy institution or modification (BP > = 140/90 mmHg) synchronous 24hABPM was actually normal (<130/80 mmHg) while in additional 124 visits (16% of all visits) 24hABPM was in the hypertensive range while office BP was in the normotensive range. Overall, in 40% of visits office BP provided misleading therapeutic indications.

Conclusions: Hypertension misclassification by office BP is a pervasive phenomenon in stable renal transplant patients on long term follow up. Office BP may lead to inappropriate therapeutic decisions in 40% of follow up visits in these patients. Periodic application of 24hABPM for the management of renal transplant patients should be formally recommended in this population.

EXOSOMAL MICRORNA PROFILE IN HYPERTENSIVE PATIENTS WITH ALBUMINURIA

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Objective: Urinary albumin excretion (UAE) is an indicator of early renal and cardiovascular damage. MicroRNAs (miRNA) are small non-coding RNAs that regulate gene expression and changes in the miRNA levels in biofluids have been related to several pathophysiological conditions. Recently, exosomes (small membranous vesicles of 40–130 nm) have been described as new biological effectors able to transport nucleic acids, proteins and lipids between cells. The aim of this work was to identify the exosomal miRNAs associated to the presence of albuminuria in hypertension.

Design and method: This prospective study analyzed 52 hypertensive patients, 24 with microalbuminuria (UAE = 162,8 ± 168.2 mg/g creatinine; mean age 52.7 ± 8.4 years) and 28 normoalbuminuric (mean age 54.5 ± 5.6 years). Exosomes were isolated by differential ultracentrifugation from urine and plasma. After RNA isolation, we prepared individual libraries for small RNAs and sequence them by next-generation sequencing. MiRNA over-representation and enrichment analysis were performed in order to identify the most regulated biological processes (KEGG pathway database). Validation was performed by RT-qPCR and miR-26a-5p levels were correlated to UAE.

Results: We found a signature of 29 exosomal miRNAs differentially expressed in response to microalbuminuria. The most regulated biological processes by the miRNAs obtained were cell signaling (MAPK, calcium, p53), TGF-beta and VEGF pathways, cytokine-cytokine receptors, regulation of actin cytoskeleton, cell cycle and apoptosis, cell junctions and extracellular matrix molecules and interactions. Particularly, only miR-26a-5p was found altered (down-regulated, 4-fold change) in both urine and plasma exosomes. We validated a decrease in the levels of miR-26–5p in urinary exosomes of microalbuminuric patients (4.7- fold change, $p < 0.05$). Finally, miR-26a-5p copy number correlated inversely with UAE levels ($r = –0.546$, $p < 0.05$).

Conclusions: Our results show an exosomal miRNA signature associated to microalbuminuria in hypertension. Interestingly, miR-26a-5p is decreased in urinary exosomes of microalbuminuric patients. This miRNA appears to be regulating VEGF and TGF-beta, key molecules in the development and maintenance of glomerular filtration barrier. The identified miRNAs may shed new light on how albuminuria develops and progress in hypertension.

HYPERTENSION AND RENAL FUNCTION IMPAIRMENT IN LOW-GRADE RENAL ARTERY STENOSIS

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Objective: after the disappointing results of the stent trials, a certain nihilism has entered the diagnostic workup of Atherosclerotic Renal Artery Stenosis (ARAS). However, by nature, no improvement could have been expected in the end stage atherosclerotic disease, which we believe severe ARAS represents. In current conception of clinically relevant renal artery stenosis, there is no consensus on a threshold for stenosis severity. Nonetheless, in guidelines for revascularization emphasis remains on severe (>70%) renal artery stenosis. Data supporting this approach are scarce. We hypothesize that renal artery stenosis is associated with hypertension and impaired renal function disease long before reaching a threshold of 70% stenosis.

Design and method: in this retrospective single centre cohort, 382 patients who underwent CTA (CT scanning-angiography) were included. Their scans were reviewed and they were categorized as having no-, mild (1–30%, moderate (31–70%) or severe (>71%) renal artery stenosis. Their medical records were scrutinized to determine information about hypertension, number of antihypertensive drugs, renal function and medical history of cardiovascular disease.

Results: moderate renal artery stenosis is associated with a greater prevalence of hypertension (83%) than mild stenosis (65%) or no stenosis (41%). In concordance, eGFR is lower in moderate stenosis (68 ml/min) than mild stenosis (76 ml/min) or no stenosis (77 ml/min).

Conclusions: these results show that moderate renal artery stenosis is associated with a greater hypertension prevalence and more renal impairment. Considering this and keeping in mind that severe ARAS represents end stage atherosclerotic disease, we argue that moderate renal artery stenosis should be considered for revascularization. In moderate renal artery stenosis, effects of stenting combined with medical therapy could be more pronounced and may exert more longstanding effects.

EFFECT OF TREATMENT WITH ALLOPURINOL ON MARKERS OF MICROINFLAMMATION AND VASCULAR DAMAGE AND REPAIR IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND ASYMPTOMATIC HYPERURICEMIA

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Objective: Asymptomatic hyperuricemia (AH) is common in patients with chronic kidney disease (CKD). However, in patients with CKD the effects of AH treatment on the mechanisms of vascular damage and repair are unknown.

Objective: To study the effect of inhibition of xanthine oxidase with allopurinol on the mechanisms of vascular injury and repair in patients with CKD and AH, evaluating the effect on markers of vascular damage and repair, oxidative stress and microinflammation.

Design and method: Randomized clinical trial, double-blind, placebo-controlled, crossover design with 4-week treatment period with either allopurinol 100 mg orally daily or placebo, 4-week wash-out period and 4-week period of treatment with placebo or allopurinol. Studies performed at first and last visit of each treatment period: 1) vascular damage and repair mechanisms markers: microparticles derived from endothelial cells (MPs), circulating endothelial progenitor cells (EPCs), vascular growth factors, 2) oxidative stress: xanthine oxidase and superoxide dismutase and 3) microinflammation: monocytes subpopulations and cytokines.

Results: 23 patients finished the study (65.2% men, age 57.52 ± 11.75 years, baseline MDRD-4 42.1 ± 11.2 ml/min/1.73 m2, urinary albumin/creatinine ratio 0.29 ± 0.39 mg/mg and serum uric acid levels of 8.3 ± 1 mg/dl). There were no differences in baseline uric acid levels at the start of each study period. Treatment with allopurinol significantly reduced serum uric acid levels to 7 ± 1.1 mg/dl ($p < 0.05$). Treatment with placebo did not reduce uric acid levels (baseline 8.7 ± 1.5 mg/dl, final 8.5 ± 1.3 mg/dl, NS). Allopurinol induced a reduction in xanthine oxidase of 2 ± 24.1% versus a placebo increase of 12.8 ± 29.6% ($p = 0.03$). No effect was observed on superoxide dismutase, MPs and, percentage of CD14 / CD16 monocytes subpopulations, vascular growth factors, interleukins and chemotactic factors.

Conclusions: In patients with CKD and AH, 100 mg of allopurinol daily for 4 weeks compared to placebo did not induce significant changes in mechanisms of vascular damage and repair, oxidative stress and microinflammation.

EPICARDIAL FAT THICKNESS IN PATIENTS WITH AUTOSOMAL DOMINANT POLYCISTIC KIDNEY DISEASE

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Objective: Autosomal dominant polycystic kidney disease (ADPKD) is associated with early organ damage such as left ventricular hypertrophy (LVH) and higher cardiovascular risk when compared to essential hypertension (EH). Epicardial adipose tissue (EAT) is a new cardiovascular risk factor, but its correlation with

LVH in ADPKD is unknown. We sought to evaluate the correlation of ultrasound measured EAT and LVH in a well-studied group of hypertensive patients with ADPKD in comparison with essential hypertension (EH) subjects.

Design and method: We performed ultrasound measurement of the EAT and other echocardiographic parameters, such as left ventricular mass (LVM), left ventricular mass indexed by body surface area (LVMi), and left atrium size in 41 consecutive hypertensive patients with ADPKD, compared to 89 EH patients.

Results: EAT was significantly higher in ADPKD group respect to EH subjects (9.2 ± 2.9 mm vs 7.8 ± 1.6 mm, $p < 0.001$), and significantly correlated with LVM, LVMi and left atrium size in the ADPKD group ($r = 0.56$, $p = 0.005$; $r = 0.424$, $p = 0.022$; and $r = 0.48$, $p = < 0.001$, respectively). Comparing EAT against body mass index (BMI), waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP) and age, we found that EAT is the strongest predictor of LVMi ($B = 0.59$, $p = 0.036$).

Conclusions: Our data shows that EAT is higher in ADPKD patients than in EH subjects and independently correlates with LVMi. EAT measurement can be as useful marker in the cardiovascular risk stratification in ADPKD.

ORAL SESSION

ORAL SESSION 4B:
THERAPEUTICS AND CLINICAL TRIALS

GENERIC VS BRAND-NAME DRUGS FOR THE TREATMENT OF HYPERTENSION

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Objective: Although antihypertensive generics and their brand-name counterparts are bioequivalent, their equivalence in lowering blood pressure and controlling hypertension is still debated. We thus, sought to compare the effect of generic and brand-name drugs in hypertensive patients.

Design and method: We conducted an open crossover randomized controlled trial (NCT02853045) in which patients were allocated to take their usual antihypertensive treatment either exclusively with brand-name drugs for 6 weeks and then to switch for generics for another 6 weeks or following the opposite order. 24 h ambulatory blood pressure (ABP) was monitored twice, at the end of each 6-weeks period. We tested the hypothesis that generics were not worse than branded antihypertensive drugs for controlling hypertension with a non-inferiority margin of 7 mm Hg.

Results: Forty Three patients (mean age of 61 +/- 12 years, 73% male, 35% of kidney transplant patients) were included. 60% of them were under triple antihypertensive treatment (angiotensin renin blockers and channel calcium blockers being taken by 88% and 72% of the patients, respectively). Mean 24 h ABP was 129/77 mmHg and 128/77 mmHg for patients under generics and branded drugs, respectively. 58% (n = 25) of patients presented optimal BP with generics vs 69% (n = 30) with brand-name drugs. 18% (n = 8) of patients presented resistant hypertension with generics vs 11% (n = 5) with branded drugs. The differences of proportion were not statistically significant. Non-inferiority was confirmed in all subgroup analyses independently of age, gender, number of medications, severity/resistance of hypertension and dipper status. Reported adverse events were not different in nature and in frequency between generic and branded drugs.

Conclusions: Our findings support the notion that generics are not inferior than brand-name antihypertensive agents and can be safely used at least for the control of blood pressure.

CHEMICAL RENAL DENERVATION WITH ALCOHOL – LONG TERM RESULTS FROM THE PEREGRINE POST-MARKET STUDY

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Objective: The Peregrine post-market study is a prospective, single arm, open label, multicenter European trial evaluating the safety and performance of the Peregrine SystemÔ Infusion Catheter (Ablative Solutions, Inc., Palo Alto, CA, USA) to perform chemical (alcohol) renal denervation (cRDN) to treat resistant hypertension (rHTN)

Design and method: The trial allows treatment of up to 60 patients at up to 10 centers in Europe. Eligible patients have rHTN. Patients with white coat rHTN are excluded. After confirmation of anatomical eligibility, patients undergo bilateral cRDN with 0.6 mL of alcohol per renal artery using the Peregrine catheter. Major safety endpoints are assessed at 1 month. The major efficacy endpoint is the reduction of 24-hour mean (SABP) at 6 months, compared to baseline. It is anticipated that the at least 35 patients with BP data from 1 through 12 months will be presented.

Results: Treated patients (61% of males) had a mean age of 55 yo, mean BMI of 32 ± 6 kg/m2 and mean eGFR of 85 ± 18 ml/min/1,73m2. At baseline, mean Systolic Office blood pressure (SOBP) and mean SABP were 173 ± 16 mmHg and 153 ± 14 mmHg respectively (n = 31). All procedures were technically successful, with a mean procedure time of 7 ± 3 minutes/artery (n = 65). Two minor renal artery dissections that resolved without intervention and three (9%) vascular access site complications without sequelae were reported. There were no deaths, myocardial infarctions, strokes, transient ischemic attacks or renal events. At 1-month, mean SOBP and SABP reductions were -24 ± 22 mmHg (n = 28; p < 0.001) and -11 ± 13 mmHg (n = 26; p < 0.001), respectively. At 6-months, mean SOBP and SABP reductions were -18 ± 25 mmHg (n = 21; p = 0.002) and -14 ± 16mmHg (n = 21; p = 0.005), respectively. In 2 of 28 patients (7%) antihypertensive medications were reduced at 1 month and in 3 of 24 patients (12%) at 3 months. In a single patient, antihypertensive medications were increased at 6 months. This abstract serves as a promissory for updated data to be presented

Conclusions: Chemical RDN using the Peregrine catheter is feasible, safe and accompanied by a significant BP reduction. Additional data from larger randomized, double-blind, clinical trials will be needed to confirm these results.

EFFECT OF RESVERATROL ON BLOOD PRESSURE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, CONTROLLED, CLINICAL TRIALS

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Objective: We aimed to assess the impact of resveratrol on BP through systematic review of literature and meta-analysis of available randomized, controlled clinical trials (RCTs).

Design and method: Literature search included SCOPUS, PubMed-Medline, ISI Web of Science and Google Scholar databases up to 17th October 2017 to identify RCTs investigating the impact of resveratrol on BP. Two review authors independently extracted data on study characteristics, methods and outcomes. Overall, the impact of resveratrol on BP was reported in 17 trials.

Results: Administration of resveratrol did not significantly affect neither systolic BP [weighted mean difference (WMD): -2.5 95%CI:(-5.5, 0.6) mmHg; p = 0.116; I2 = 62.1%], nor diastolic BP [WMD: -0.5 95%CI:(-2.2, 1.3) mmHg; p = 0.613; I2 = 50.8], nor mean BP [MAP; WMD: -1.3 95%CI:(-2.8, 0.1) mmHg; p = 0.070; I2 = 39.5%] nor pulse pressure [PP; WMD: -0.9 95%CI:(-3.1, 1.4) mmHg; p = 0.449; I2 = 19.2%]. However, significant WMDs were detected in subsets of studies categorized according to high resveratrol daily dosage (more than 300 mg/day) and presence of diabetes. Meta-regression analysis revealed a positive association between systolic BP-lowering resveratrol activity (slope: 1.99; 95%CI: 0.05, 3.93; two-tailed p = 0.04) and Body Mass Index (BMI) at baseline, while no association was detected neither between baseline BMI and MAP-lowering resveratrol activity (slope: 1.35; 95%CI: -0.22, 2.91; twotailed p = 0.09) nor between baseline BMI and PP-lowering resveratrol activity (slope: 1.03; 95%CI: -1.33, 3.39; two-tailed p = 0.39). Resveratrol was fairly well-tolerated and no serious adverse events occurred among most of the eligible trials.

Conclusions: The favourable effect of resveratrol emerging from the current meta-analysis suggests the possible use of this nutraceutical as active compound in order to promote cardiovascular health, mostly when used in high daily dose (over 300 mg/day) and in diabetic patients.

BENEFITS AND HARMS OF ANTIHYPERTENSIVE TREATMENT FOR UNCOMPLICATED MILD HYPERTENSION IN PRIMARY CARE: AN OBSERVATIONAL COHORT STUDY IN THE CLINICAL PRACTICE RESEARCH DATA LINK

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Objective: Evidence to support initiation of pharmacological treatment in patients with uncomplicated (low risk) mild (stage 1) hypertension is inconclusive

and clinical guidelines are contradictory. The aim of this study was to use electronic health records and statistical methods which minimise bias in non-randomised studies to examine whether treatment is safe and effective at reducing the risk of mortality and cardiovascular disease in uncomplicated mild hypertensives.

Design and method: This study had a longitudinal cohort design using electronic health records from Primary Care. Data were extracted from patients in the Clinical Practice Research Datalink from England, aged 18–74 years, with stage 1 hypertension (blood pressure between 140/90–159/99mmHg), no cardiovascular disease (CVD) risk factors and no treatment, from 1998–2015. Patients exited if follow-up records became unavailable due to death or moving away from a participating practice. Propensity scores predicting likelihood of treatment were constructed using a logistic regression model. Individuals on treatment were matched to those not on treatment 12 months after a diagnosis of hypertension, by propensity score using the nearest neighbour method. The rate of mortality, cardiovascular disease and adverse events in patients on treatment were compared to those not on treatment using Cox regression.

Results: A total of 19,143 untreated patients (mean age 54.7 ± 12.2 years, 56.0% female) were matched to 19,143 similar patients on treatment. During a period of up to 15 years follow-up, no association was found between antihypertensive treatment and mortality (HR 1.07, 95%CI 0.97–1.18), cardiovascular disease (HR 1.02, 95%CI 0.92–1.14) or any individual cardiovascular disease endpoints. Treatment was associated with an increased risk of adverse events including hypotension (HR 1.63, 95%CI 1.34–1.97), syncope (HR 1.26, 95%CI 1.12–1.42), electrolyte abnormalities (HR 1.50, 95%CI 1.09–2.07) and acute kidney injury (HR 1.41, 95%CI 1.13–1.76).

Conclusions: This appropriately powered study found no evidence to support the initiation of antihypertensive treatment in patients with uncomplicated mild hypertension. However, there was evidence of an increased risk of adverse events and clinicians should refrain from using treatment in this population, since it may do more harm than good.

COMPARATIVE EFFICACY OF ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS II IN ESSENTIAL HYPERTENSION: SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Objective: Angiotensin converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) are widely used for the treatment of hypertension. However, data on their comparative efficacy is incomplete. The present systematic review and network meta-analysis investigated the comparative efficacy of these two drug categories in blood pressure reduction, mortality and morbidity of adults with essential hypertension.

Design and method: Bibliographic search was performed in Medline (PubMed) and Cochrane Central Register of Controlled Trials (CENTRAL) for placebo- and active-controlled, double-blind randomized trials, which had studied for blood pressure reduction, mortality and/or morbidity.

Results: Thirty studies with 7370 participants were included for the blood pressure reduction analysis and eight studies with 25158 participants were included for the mortality/morbidity analysis. The two pharmacological categories did not differ in lowering systolic (WMD: 0.59, 95%CI: -0.21 to 1.38) and diastolic blood pressure (WMD: 0.62, 95%CI: -0,06 to 1.30), all-cause mortality (RR: 0.96, 95%CI 0.80 to 1.14), cardiovascular mortality (RR: 0.87, 95%CI 0.67 to 1.14), fatal and non-fatal myocardial infarction (RR: 1.02, 95%CI 0.75 to 1.37) and stroke (RR: 1.13, 95%CI 0.87 to 1.46). ACEIs found to be superior in the development and/or hospitalization for heart failure (RR: 0.71, 95%CI 0.54 to 0.93).

Conclusions: ACEIs and ARBs do not differ in blood pressure reduction, mortality and morbidity in patients with essential hypertension. ACEIs were superior in the development and/or hospitalization for heart failure.

REAL WORLD EFFICACY OF NEVIBOLOL ACCORDING TO VARIOUS PRESCRIPTION PATTERNS IN THE OPEN, NON-CONTROLLED, PROSPECTIVE, MULTICENTER OBSERVATIONAL STUDY IN KOREA (BENEFIT-KOREA)

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Objective: Although the role of beta blocker in major hypertension guideline is limited, the role of vasodilating beta blocker is suggested to be different from the conventional beta blocker. Despite of many small sized studies for the pharmacological properties, there are few large sized real world data for blood pressure (BP) lowering efficacy of nevibolol in hypertension patients in Asia.

Design and method: In the open, non-controlled, prospective, multicenter observational study to identify BEnefits after 24 weeks of NEvibolol administration For essential hypertensIon patients wiTH various co-morbidities and treatment environments in KOREA (BENEFIT-KOREA), 3011 patients was enrolled and 2571 patients (85.3%) completed 24 week follow up. The efficacy of nevibolol was measured according to four prescription patterns, i.e., de novo therapy (n = 279), single drug switching (n = 257), switching for combination therapy (n = 978), and add-on therapy (n = 1057).

Results: Age was 63.5 ± 12.9. Female was 40.4% and the elderly aged > 65 was 52.7%. Dyslipidemia, obesity, and diabetes mellitus were noted in 50.5%, 37.4%, and 28.9%. Co-morbidity was noted in 89.1% and majority was ischemic heart disease. Concomitant medication rate for calcium antagonist, ARB/ACEI, diuretics were 54.3%, 53.5/9.2%, and 23.7%. Median dosage of nevobolol was 5 mg. For de novo therapy, BPs decreased from 142.4/84.9 mmHg to 127.9/75.1 mmHg (-13.9/-9.5 mmHg, $p < 0.0001$). For single drug switching group, BPs decreased from 134.3/78.7 mmHg to 127.1/75.3 mmHg (-7.5/-3.6 mmHg, $p < 0.0001$). For switching for combination therapy group, BPs decreased from 137.8/80.1 mmHg to 131.6/76.6 mmHg (-6.4/-3.6 mmHg, $p < 0.0001$). For add-on therapy group, BPs decreased from 146.0/85.5 mmHg to 130.9/76.3 mmHg (-15.0/-9.1 mmHg, $p < 0.0001$). Adverse drug reaction was noted in 1.2%.

Conclusions: Nevibolol was demonstrated to be a comparable drug for switching in single or combination therapies and to be an effective BP lowering drug for de novo or add-on therapies in a real world Asian hypertension patient with aging, cardiovascular risk factors, and co-morbidities.

PHARMACO-METABOLOMICS OF BLOOD PRESSURE RESPONSE TO BETA-BLOCKERS AND DIURETICS

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Objective: Pharmacometabolomics have shown promise in identifying small molecule markers for drug response. In the current study, we propose to identify pre-treatment metabolomic markers of anti-hypertensive drug response in two multi-ethnic RCTs of mono-therapy with hydrochlorothiazide, atenolol, metoprolol, and chlorthalidone.

Design and method: The PEAR (Pharmacogenomic Evaluation of Antihypertensive Responses) and PEAR 2 studies were prospective, multi-centre studies of two anti-hypertensive drugs in subjects with uncomplicated mild to moderate essential hypertension. Subjects were randomised to one of two treatment arms (atenolol and hydrochlorthiazide) in PEAR, or underwent sequential monotherapy with metoprolol followed by chlorthalidone (PEAR 2). LC/MSMS metabolomics of baseline plasma samples were performed by Metabolon Inc. Blood pressure response (BPR) was calculated as the difference between blood pressure during and before treatment. Metabolite BPR association was tested by linear regression

adjusted for age, sex, ethnicity, BMI, study site and baseline BP. Family Wise Error Rate (FWER) was controlled conservatively using Holm correction.

Results: 2-hydroxyglutarate (2-HG) strongly associated with diastolic BPR to hydrochlorothiazide (Holm p-value = 0.00045). Diastolic and systolic BP were both predicted to rise 2.2 mmHg per standard deviation increase in pre-treatment 2-HG quantile normalised level. For systolic BPR the effect was nominally significant. No other drug associated with 2-HG. The most significant BPR ethnicity by metabolite interaction was for vanillylmandelate (VMA) and diastolic BPR to atenolol (Holm p-value = 0.047). It predicts an extra 7.1 mmHg diastolic BP drop in whites compared to blacks, per standard deviation increase in pre-treatment VMA quantile normalised level. The systolic BPR interaction was almost as significant.

Conclusions: Systematic metabolomic analyses identified 2-hydroxyglutarate as a predictor of hydrochlorothiazide response and ethnicity specific effect of VMA on atenolol response.

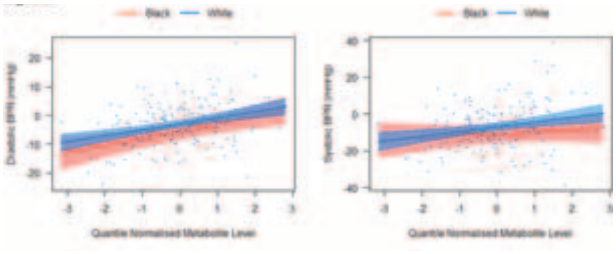

Figure 1 Scatterplots of hydrochlorothiazide BPR versus quantile normalised 2-hydroxyglutarate level in pre-treatment plasma. Left/right – diastolic/systolic BPR. Red/blue – prediction line, 95% confidence band, and partial residuals for subjects self-identifying as black/white.

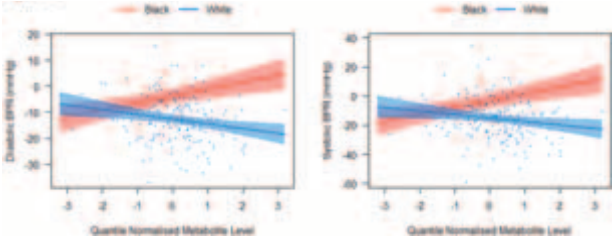

Figure 2 Scatterplots of atenolol BPR versus quantile normalised vanillylmandelate (VMA) level in pre-treatment plasma. Left/right – diastolic/systolic BPR. Red/blue – prediction line, 95% confidence band, and partial residuals for subjects self-identifying as black/white.

ORAL SESSION

ORAL SESSION 4C:
CEREBROVASCULAR DISEASE, STROKE AND COGNITIVE DYSFUNCTION

CLINICAL CHARACTERISTICS OF PATIENTS WITH SPONTANEOUS CERVICAL ARTERY DISSECTION - THE POLISH REGISTRY FOR FIBROMUSCULAR DYSPLASIA (ARCADIA-POL STUDY)

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Objective: To assess the clinical characteristics of consecutive patients with spontaneous cervical artery dissection enrolled into ARCADIA-POL study.

Design and method: Out of 250 patients enrolled into ARCADIA-POL study since January 2015 (instituted on the basis of Polish-French collaboration) we present 35 consecutive patients with confirmed spontaneous cervical artery dissection which was one of the inclusion criteria to the study. A standardized FMD data form was used for data collection. All patients underwent detailed clinical evaluation including ABPM, biochemical evaluation, biobanking, duplex Doppler of carotid and abdominal arteries and whole body angio-CT.

Results: In our analysis we included 35 patients with confirmed spontaneous cervical artery dissection (27F [68.6%], 11 M [31.4%], mean age: 44.6 ± 8.45 years). 23 (65.7%) patients had internal carotid and 10 (28.6%) had vertebral artery dissection. In two patients carotid and vertebral artery dissections coexisted. Fibromuscular dysplasia (FMD) was confirmed in 13 (37.1%) patients – in 8 patients in one and in 5 patients in two vascular beds. Among patients with cervical artery dissection coexisting with FMD, the most frequent localization of FMD lesions were carotid arteries (61.5%) and renal arteries (38.5%). 20 patients out of 35 (57.1%) were hypertensives with the mean office blood pressure values of 128 ± 19/81 ± 11 mmHg and daytime ABPM values of 129 ± 15/83 ± 10 mmHg on the median number of one antihypertensive agent. 7 patients (20%) were smokers. The most frequent clinical symptoms associated with the occurrence of cervical artery dissection in the analyzed group were headaches (68.6% patients), vision disturbances (45.7% patients), Horner's syndrome (40% patients), dizziness (40% patients), eye pain(40% patients), and neck pain (31.4% patients). In 14 patients (40%) cervical artery dissection was associated with ischemic stroke and in 5 patients (14.3%) with transient ischemic attack. There was no associated hemorrhagic brain complications observed.

Conclusions: Our data indicate that in patients with spontaneous cervical artery dissection FMD is present in one third of cases. This group is characterized by relatively high prevalence of hypertension and in more than half of the cases spontaneous cervical artery dissection resulted in acute cerebrovascular event or ischemic stroke.

HIPPOCAMPAL CEREBRAL BLOOD FLOW DEPENDS ON SYSTEMIC ENDOTHELIAL FUNCTION IN INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENT: THE TRAIN, THE BRAIN-MIND, THE VESSEL STUDY

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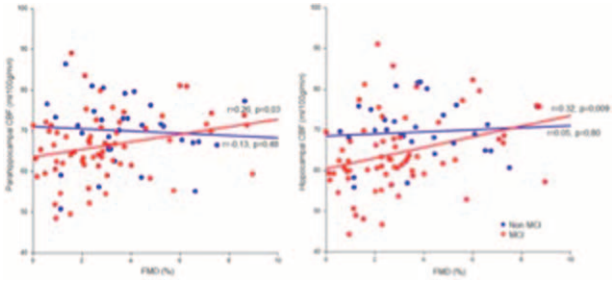
Objective: Dementia has been recently viewed as a predominantly vascular disorder. Indeed, reduced brain NO availability causes increased ß-amyloid deposition by several mechanisms, including hypoperfusion. We sought to investigate the relationship between cerebral blood flow in the hippocampal and parahippocampal regions (CBF-hipp and CBF-parahipp), crucial areas for memory and processing of non-verbal/spatial information, and systemic endothelial function in individuals with mild cognitive impairment (MCI), a subclinical condition predisposing to dementia.



Design and method: CBF-hipp and CBF-parahipp were evaluated by magnetic resonance imaging (arterial spin labeling, GE HDxt 1.5 T Signa Neuro-optimized System) and systemic endothelial function by flow-mediated dilation (FMD) in the brachial artery.

Results: Complete data about CBF and FMD at enrollment were available for 66 individuals with MCI and 32 without (non-MCI). The two groups were matched for age (75 ± 5 vs 74 ± 5years, p = 0.22), sex (men 45 vs 50%, p = 0.18) and mean BP (96 ± 10 vs 97 ± 9mmHg, p = 0.41). FMD was significantly lower in MCI than in non-MCI (2.93 ± 2.18 vs 3.74 ± 2.03%, p = 0.02); CBF-hipp (64.3 ± 9.43 vs 69.5 ± 7.03 ml/100 gr/min, p = 0.002) and CBF-parahipp (66.3 ± 8.02 vs 70.0 ± 8.12 ml/100 gr/min, p = 0.002) were significantly lower in MCI as well. Among MCI, FMD was significantly correlated with CBF- parahipp (r = 0.26,p = 0.03) and CBF-hipp (r = 0.32,p = 0.009). In multiple regression models, including age, sex, mean BP, BMI, brachial artery diameter as confounders, FMD remained an independent determinant of CBF-parahipp (beta = 0.93, r2 = 0.063, p = 0.04) and CBF-hipp (beta = 1.31, r2 = 0.089, p = 0.01). Nor CBF-parahipp (r = –0.13, p = 0.48) neither CBF-hipp (r = 0.05, p = 0.80) were correlated with FMD in non-MCI group.

Conclusions: An independent association between hippocampal and parahippocampal CBF and systemic endothelial function is present in individuals with MCI.

SHORT-TERM FUNCTIONAL OUTCOME AFTER ISCHEMIC STROKE IS RELATED TO BLOOD PRESSURE VARIABILITY

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Objective: Stroke is the second most common cause of death. Although one of the most important stroke causes is hypertension, the prognostic value of blood pressure (BP) variability in stroke victims remains inconsistent. The aim of the study was to assess the relationship between blood pressure variability and functional outcome after ischemic stroke.

Design and method: We analysed 94 patients with acute ischemic stroke admitted to the Department of Adult Neurology, Medical University of Gdansk, Poland. Ambulatory blood pressure monitoring (ABPM) was performed one week after stroke. ABPM-based coefficients of variation (CV, standard deviation/mean x100) for systolic (SBP), mean (MBP), and diastolic (DBP) BP were calculated. Short-term functional outcome was evaluated at day 7 with modified Rankin Scale (mRS) score of 0 to 1 defined as excellent outcome. BP variables were compared between excellent and non-excellent groups; possible co-founders were included in multivariate logistic regression.

Results: The mean patient age was 68.0 (±12.4) years. In univariate analysis, CVs for DBP and MBP were higher in the excellent group (13.5 vs. 12.2, p = 0.02; 11.6 vs. 10.4, p = 0.01; respectively; Table 1). In multivariate logistic regression, after adjustment for age, sex, National Institutes of Health stroke scale (NIHSS)

score, previous stroke, and tissue plasminogen activator administration (tPA), the relationship remained statistically significant (Tables 2 and 3).

Table 1.

	mRS 0-1	mRS>1	p value
CV for SBP	10.0±2.5	9.2±2.6	0.17
CV for DBP	13.5±2.7	12.2±2.7	0.02
CV for MBP	11.6±2.2	10.4±2.4	0.01

Table 2.

	NIHSS	Age	Sex	Previous stroke	tPA	CV for DBP
p	<0.01	0.37	0.41	0.15	0.25	0.03
Odds ratio	0.77	0.98	1.61	0.33	2.04	1.25
95% confidence interval	0.66-0.90	0.94-1.02	0.51-5.08	0.07-1.52	0.60-6.91	1.02-1.53

Table 3.

	NIHSS	Age	Sex	Previous stroke	tPA	CV for MBP
p	<0.01	0.28	0.51	0.16	0.14	0.01
Odds ratio	0.76	0.98	1.46	0.33	2.49	1.37
95% confidence interval	0.65-0.89	0.93-1.02	0.46-4.66	0.07-1.54	0.73-8.49	1.07-1.76

Conclusions: Blood pressure variability measured as CVs for DBP or MBP was associated with early functional outcome after ischemic stroke independently of classical predictors.

HIPPOCAMPUS VOLUMETRY AND VASCULAR DAMAGE IN A COHORT OF OLDER PATIENTS WITH HYPERTENSION: INSIGHTS FROM THE ADELAHYDE STUDY

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Objective: Hypertension has been considered as a modifiable risk factor associated with the development of dementia. Various indices of micro- and macro-circulation have been correlated with progressive Alzheimer's disease, but little is known about their association with hippocampal atrophy, especially in the early stages of the disease. The aim of this study is to investigate the association between hippocampal volume (HV) and cardiovascular risk factors in a cohort of individuals from the ADELAHYDE, a longitudinal study, investigating the role of vascular factors in the evolution of cognitive functions in a cohort of treated hypertensive patients over 60 years without dementia at inclusion, who were evaluated at inclusion (V1) and after 8 years (V2).

Design and method: HV was measured automatically in brain MRIs with Free Surfer Software during V2 in all subjects who have participated to both visits of the ADELAHYDE study. A detailed medical history, somatometric measurements, cognitive tests, leukoraiosis severity (Fazekas score), vascular parameters including pulse wave velocity, central blood pressure and carotid artery plaques,as well as several biochemical parameters were also measured.

Results: In the study participated 113 hypertensive patients, 47% male, aged 75.1 ± 5.6 years. At V2 in the multivariate model, male sex (p = 0.009), older age (p = 0.004), lower BMI (p = 0.025), longer duration of hypertension (p = 0.014) and a higher Fazekas score (p = 0.018) and a reduced Cognitive Test Score (p = 0.002), were all independent predictors of lower HV. The total model was able to explain 36.2% of the variation of the hippocampal volume. No association was observed between HV and aortic stiffness of carotid artery geometry. The V1 predictors of lower HV at V2 were older age (p = 0.001), male sex (p = 0.006) and duration of hypertension (p = 0.026).

Conclusions: Age, sex, BMI, duration of hypertension, cognitive decline and microvascular cerebral status (leukoaraiosis), were independent factors of HV. Future studies could investigate whether the preventive strategies against these factors could prevent hippocampal atrophy and delay or even reverse the progression and its clinical consequences.

THE EFFECT OF ANTIHYPERTENSIVE TREATMENT ON THE PREVALENCE OF ORTHOSTATIC HYPOTENSION IN ALZHEIMER'S DISEASE: SECONDARY ANALYSES OF A RANDOMIZED CONTROLLED TRIAL (NILVAD TRIAL)

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Objective: Hypertension is a common comorbidity among patients with Alzheimer's disease (AD), but guidelines advice to be cautious in prescribing antihypertensive treatment, a.o. because a perceived increased risk of orthostatic hypotension (OH). However, this has never been examined prospectively in a trial. We aimed to investigate whether the calcium-channel antagonist nilvadipine increases the prevalence of OH in patients with AD.

Design and method: A double-blind, placebo-controlled trial (NILVAD) was performed at 23 sites and included 511 patients with mild to moderate AD (NIA-AA criteria), aged > 50 years, with baseline blood pressure (BP) between 100–159 mmHg systolic and 65–99 mmHg diastolic. Patients were randomized to 8 mg nilvadipine or placebo, daily, for 78 weeks. Sitting and standing BP were measured at 7 subsequent visits. Measurements were included if treatment compliance was > 79%. OH (drop of > = 20 mmHg systolic BP and/or > = 10 mmHg diastolic BP) and dSBP (sitting-standing systolic BP) were calculated. Differences between groups were compared using multilevel (logistic) regression analysis, with fixed effects for treatment and baseline OH, and random intercepts for patient and study site, using an alpha level of 0.05. The study had 80% power to detect a clinically relevant increase in OH prevalence of 10% (odds ratio 1.89).

Results: 478 patients (240 nilvadipine aged 72.4 ± 8.6 years, 238 placebo aged 71.9 ± 7.9 years) had at least 1 follow-up measurement available. Complete follow-up was available in 71.5% of patients. At baseline, mean BP was 138/77 (±14/9) mmHg in the nilvadipine group and 137/77 (±14/9) mmHg in the placebo group. Nilvadipine lowered BP with -5.2/-2.4 mmHg, compared to placebo (P < 0.001). Prevalence of OH and dSBP at baseline and per visit are shown in Figure 1. There was no effect of treatment on OH prevalence (odds ratio [95% CI] = 1.13 [0.88–1.47], P = 0.34) or dSBP (b [95% CI] = 0.66 [-0.32–1.65], P = 0.19).

Conclusions: Nilvadipine successfully lowered BP, without an increase in OH prevalence. This contradicts the view that antihypertensive treatment in patients with AD is associated with an excessive risk of OH. Planned further analyses include the risk of falls and fractures in this study.

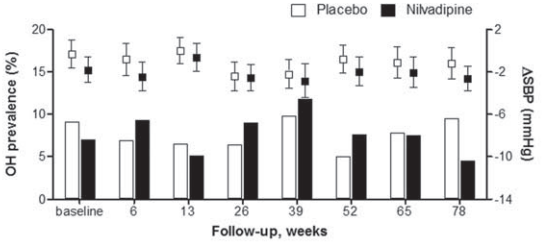

Figure 1. Prevalence of orthostatic hypotension (OH, left y-axis) and sitting minus standing systolic blood pressure (ΔSBP, right y-axis) at baseline and per follow-up visit

UTILITY OF THE CLOCK DRAWING TEST AS COGNITIVE SCREENING IN PATIENTS WITH ARTERIAL HYPERTENSION

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Objective: 1. To compare two cognitive tests, Mini-mental (MMSE) and clock drawing test (CDT), as screening tools for cognitive impairment (CI) in hypertensive patients. 2. To know the prevalence of executive dysfunction in hypertensive patients and its association with different variables (treatment and control, level of education and other cognitive proof).

Design and method: A multicentre study (18 centers) that included hypertensive patients (both sexes, > / = 18 years). Patients were divided into 3 groups: treated/controlled BP < / = 140–90 mm Hg (TC), treated/non-controlled > 140–90 mm Hg (TNC) and untreated (UT). The educational level was recorded. MMSE and CDT tests were administered (cut-off CDT 5 on 7 and MMSE according to age and education).

Results: 1414 hypertensive patients, average age 59.7 ± 13.8 years, female 62.3%. The mean BP of the sample were: SBP 143.6 ± 21.2 mm Hg, DBP 83.6 ± 12.3 mm Hg. With 7 years of education: 44.5%, between 8 and 12 years: 33% and more than 12 years: 22.4%. The average MMSE score was 26.7 ± 3.5 and the CDT 5.5 ± 1.7. The prevalence of CI evaluated by the MMSE (</ = 24): 20.7% (n = 293) and by the CDT (</ = 5): 36.1% (n = 511). Among hypertensive patients with normal MMSE (> 24) 29.3% had abnormal CDT. There was no association between the abnormal CDT and the treatment groups (TC, n = 546, 36.2%,

TNC/NT, n = 869, 36.5%, p 0.56). There was an inverse association between the level of education and the abnormal CDT (</ = 7 years education 45.8%, between 8 to 12 years 30.2% and > / = 12 years 20.8%, p 0.000). The CDT correlated positively with the attention proof (Rho 0.40 ± 0.03, p 0.000) and visuo-construction proof (pentagons) of the MMSE (Rho 0.45 ± 0.04, p 0.000).

Conclusions: The CDT is more useful tan MMSE in the cognitive screening of hypertensive patients. 1/3 of hypertensive patients with normal MMSE had abnormal CDT. The CDT was associated inversely with the educational level and positive way with the attention and visual-construction proofs of the MMSE

EFFECT OF PULSATLITY IN CENTRAL AORTA ON CEREBRAL BLOOD FLOW WITH ADVANCING AGE AND HYPERTENSION

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Objective: Increasing pulsatility in the central aorta with arterial stiffening has been suggested as a potential causative factor of age-related cerebral dysfunction associated with cognitive impairment and cerebral small vessel disease. We recently showed in a large cohort (n = 1020) that changes of pulsatile features of the central aortic pressure (cAP) waveform (eg. increase of late systolic secondary augmented pressure) with advancing age are related to corresponding pulsatile features of flow velocity (FV) in cerebral arteries. The aim of this current study was to assess the association of pulsatility of central aortic pressure (cAP) and cerebral arterial FV with age and hypertension.

Design and method: Three groups of adult subjects were studied: normotensive (NT; n = 22, age 28 ± 4.8 yrs); young hypertensive (YHT; n = 11, age 41 ± 5.4 yrs) and old hypertensive (OHT; n = 12, age 63 ± 6.2 yrs). Hypertension was defined as brachial systolic pressure > 140 mmHg or diastolic pressure > 90 mmHg. Non-invasive measurements of cAP were obtained from transformation of calibrated radial tonometry waveforms (SphygmoCor, AtCor Medical, Sydney). Cerebral FV was recorded by a transcranial Doppler device in the middle cerebral artery. Pulsatility index) was computed as the ratio of pulse to mean components of cAP (pPI) and cerebral FV (fPI).

Results: There was a significant difference in mean arterial pressure in YHT (108.5 ± 6.1 mmHg) and OHT (111.7 ± 11.8 mmHg) compared to the NT (87.2 ± 6.6 mmHg, $p < 0.05$). The associated pules pressure (mmHg) was NT:41 ± 9; YHT:56 ± 6; OHT:84 ± 34). There were no significant corresponding changes in mean FV (NT:61.1 ± 11.9 cm/s; YHT:67.2 ± 17.3 cm/s; OHT:59.6 ± 20.5 cm/s). Compared to NT, corresponding mean changes (%) of pPI and fPI were YHT: pPI = 19% ($p < 0.05$), fPI = 16% (NS); OHT:pPI = 85% ($p < 0.05$), fPI = 46% ($p < 0.05$).

Conclusions: Findings show that mean cerebral flow at rest is maintained with changes in mean systemic arterial pressure in young and old hypertensive subjects due to cerebral autoregulation. With hypertension, cerebral flow pulsatility increases with age, likely due to increased stiffness of systemic arteries. Increased pulsatility in the presence of cerebral autoregulation suggests greater exposure of resistive cerebral vasculature to deleterious effects of cyclic mechanic stress.

EFFECT OF STENTING ON BLOOD PRESSURE IN HYPERTENSIVE PATIENTS WITH SYMPTOMATIC PROXIMAL SUBCLAVIAN OR VERTEBRAL ARTERY STENOSIS

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Objective: Data from animal studies showed that the artery occlusion supplying the brainstem caused a significantly greater increase in sympathetic nerve activity and mean arterial pressure. To gain support for this hypothesis in human, We postulate that the level of blood pressure in patients with posterior circulation hypoperfusion caused by significant stenosis of the proximal subclavian or vertebral arteries may reduced after successfully stenting the lesions. To evaluate the effect of stenting on blood pressure in hypertensive patients with symptomatic proximal subclavian or vertebral artery stenosis.

Design and method: A. total of 48 patients with essential hypertension (33 males; mean age 63.0 ± 8.7 years) with symptomatic proximal subclavian or vertebral artery stenosis(diameter reduction > / = 70%), who underwent successfully stenting on the lesions, were prospectively enrolled at Fuwai Hospital between January 2014 and December 2015. All 48 patients were followed up at 1, ^{3}and 6 months after the procedure. During the study, antihypertensive agents and dosage were fixed, Blood pressure and complications were investigated.

Results: Baseline values included mean office blood pressure of 132/77 ± 10/8 mm Hg, 24-hour mean blood pressure of 127/75 ± 12/9 mm Hg, and mean of 1.6 ± 0.8 antihypertensive agents. The mean subclavian and vertebral artery stenosis decreased from 88.9 ± 9.5% and 85.8 ± 7.4% to5.5 ± 3.5% and 4.6 ± 3.7% immediately after stenting, respectively. Mean reductions in office blood pressure were –7/–3 (95% CI 3/2), –9/–4 (5/3), and –10/–5 mm Hg (7/5) at 1, 3, and 6 months, respectively. 24-hour mean blood pressures after the procedure were reduced by –5/–3 mm Hg at 6 months.No procedure related complications occurred.

Conclusions: This first prospective cohort study in human showed posterior circulation revascularization appears to be effective in reducing blood pressure in hypertensive patients with symptomatic proximal subclavian or vertebral artery stenosis. However, the finding should be confirmed further.

VASCULAR AND NON-VASCULAR PREDICTORS OF COGNITIVE DETERIORATION IN HYPERTENSIVE PATIENTS

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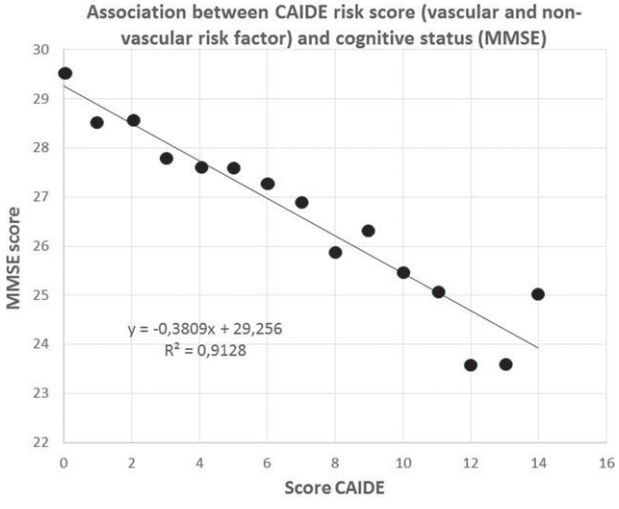
Objective: Hypertension (HTN) is the main vascular risk factor for developing cognitive impairment (CI) and dementia, but there are other vascular and non-vascular risk factors that increase this risk. 1)To know the current cognitive status and to stratify the risk of dementia in a sample of hypertensive patients, 2) to observe the association between vascular and non-vascular risk factors with the current cognitive status.



Design and method: Hypertensive patients participants from the Heart-Brain Study in Argentina (both sexes, > 21 years). To assess the current cognitive status, the Mini-mental test (MMSE) adjusted to age and level of education was used. And, to stratify the risk of dementia, the CAIDE score (Cardiovascular risk, aging and incidence of dementia) was used for assesses the risk factors: 1) non-modifiable (age and sex), 2) modifiable non-vascular (education) and 3) modifiable vascular (hypertension, obesity, cholesterol and physical activity)

Results: Were included 1279 hypertensive patients, average age 60.2 ± 13.5 years (71% female). The average years of education of the total sample was 9.9 ± 5.1 years. With 7 years or less of education: 44.5%; between 8 and 12 years old: 33% and 12 years old or more: 22.4%. The 46% of the sample were treated and controlled. The average MMSE score in the total sample was 26.6 ± 3.6 pts (Normal (27–30 pts) 66.3%, doubtful (25–26 pts) 10.6% and abnormal (< / = 24) 21.1 %. According to the CAIDE score, 55.4% presented a low risk of dementia (1 to 1.9%), 39.7% moderate risk (4.2 to 7.4%) and 4.7% high risk (16.4%). An inverse relationship was observed between CAIDE score (vascular and non-vascular risk factors) and current cognitive status (MMSE) (R2 0.9128, p 0.000).

Conclusions: Cognitive impairment (MMSE < / = 24 pts) was present in more than 20% of hypertensive patients. Approximately 40% of hypertensive patients presented a moderate risk of dementia and 5% severe risk. The CAIDE score (vascular and non-vascular risk factors) was inversely related to the current cognitive status (MMSE).

ORAL SESSION

ORAL SESSION 5A:
LIFESTYLE CHANGES, LIPIDS, SALT

ISOLATED NOCTURNAL HYPERTENSION HAD HIGHER 24-HOUR URINE SODIUM/POTASSIUM RATIO THAN NORMOTENSION

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Objective: Only few studies showed the association of salt intake with nocturnal blood pressure (BP). However, little is known about salt intake in patients with isolated nocturnal hypertension.

Design and method: Among the 1128 participants, 740 participants who had complete 24-hour urine collection and valid 24-h ambulatory BP monitoring were analyzed. Participants were grouped in 4 groups: normotension (NT, n = 371), isolated daytime hypertension (IDHT, n = 26), isolated nocturnal hypertension (INHT, n = 177), and both-hypertension having both daytime and nocturnal hypertension (both-HT, n = 166).

Results: The 24-hour urine sodium (24HUNa) was 155.4 ± 62.9, 164.1 ± 65.5, 169.8 ± 65.8 and 180.0 ± 72.2 mmol/24 hour, respectively. The 24-hour urine potassium (24HUK) was 56.6 ± 19.7, 51.3 ± 14.7, 60.1 ± 25.4 and 60.1 ± 21.4 mmol/24-hour and the 24-hour urine sodium/potassium ratio (24HUNa/24HUK) were 2.9 ± 1.2, 3.3 ± 1.0, 3.3 ± 3.2 and 3.2 ± 1.3, respectively. Compared to NT group, INHT had higher 24HUNa ($p = 0.014$), and both-HT had higher 24HUNa and 24HUNa/24HUK ($p < 0.001$ and 0.016, respectively). There was no difference in 24HUNa, 24HUNK and 24HUNa/24HUK between INHT and both-HT. In multivariate analysis controlled with age, gender, body mass index, estimated glomerular filtration rate, and use of diuretics, INHT showed significantly higher 24HUNa/24HUK than NT ($p = 0.038$). The difference of 24HUNa and 24HUNa/24HUK between NT and both-HT was not persistent in multivariate analysis.

Conclusions: The result of present study suggests that high ratio of sodium/potassium intake may be a risk of isolated nocturnal hypertension.

BLOOD PRESSURE CHANGES IN AFRICAN MALES DURING APPLICATION FOR ASYLUM STATUS IN ITALY: A PILOT STUDY

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Objective: The Central Mediterranean route from Libya to Italy has become the major port of entry to Europe for migrants and refugees. In Italy few studies analysed health of asylum seekers, being mainly focused on infectious diseases. The aim of the present study was to explore cardiovascular risk factors of young asylum seekers during their first phase of residence in Italy

Design and method: Cross-sectional study performed on male African migrants, aged 18–35 years, during the period of application for asylum status in Prato, Italy. Subjects were classified in two groups according to their months of stay in Italy. Variables (Table 1) were measured with validated instruments according to guidelines. The relationship with months of stay in Italy (independent variable) was investigated with stepwise linear regression

Results: Subjects characteristics are reported (Table 1). After 6 months, 11 subjects had impaired fasting glucose (FG > 100 mg/dL) (3 in the < 6mo Group) (RR 3.4; 95%CL 1.0 to 11.5). The significant increase of systolic BP (months as the independent variable) was selected at stepwise multivariable adjusted linear regression (B 0.154;95%Cl 0.003 to 0.305, $p = 0.046$). https://services.aimgroup.eu/ASPClient/files/3647/Abstract/584_20180112140808.jpg

Conclusions: The syndromic surveillance system now active in immigration centres in Italy is mainly focused on infectious diseases. When considering the importance of hypertension for African descendent living in Europe, changes of CV risk factors in the new environment probably need more attention

Variable	All(n=91)	≤6m(n=44)	>6m(n=45)	P
Age (years)	23.5±4.9	23.1±5.3	23.9±4.9	ns
Months in Italy	9.3±6.7	3.8±1.5	14.3±5.5	<0.05
Systolic BP (mmHg)	117±12	114±11	120±14	<0.05
Diastolic BP (mmHg)	73±9	71±9	74±10	ns
Body mass index (kg/m²)	22.3±2.7	21.9±2.6	22.6±2.7	ns
Waist circumference (cm)	83.6±8.8	84.1±8	83±9.4	ns
Haemoglobin (g/l)	14.9±1.4	14.7±1.8	15.1±0.9	ns
Fasting glucose (mg/dl)	86.6±12.6	84.7±13.4	91.1±12.1	<0.05
Triglycerides (mg/dl)	175±29	167±27	184±32	ns
Total cholesterol (mg/dl)	125±67	119±43	131±88	<0.05

RANDOMIZED STUDY OF THE EFFECTS OF COCOA-RICH CHOCOLATE ON THE VASCULAR FUNCTION AND THE VENTRICLE-ARTERIAL COUPLING OF YOUNG AND HEALTHY ADULTS

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Objective: The purpose of this study was to evaluate and explore the benefits of long-term dark chocolate intake in young healthy adults by measuring cardiovascular function.

Design and method: A randomized study was conducted in 30 healthy participants aged 18 to 27 years. Half of the participants ingested a 20 g dose of low cocoa chocolate (LCC:~55%; 12,61 ± 1,35 mg equivalent of epichatequin/g) and the others ingested a daily dose of 20 g of high cocoa chocolate (HCC:~90%; 18,19 ± 2,64 mg equivalent of epichatequin/g). A baseline evaluation was performed before the participants started ingesting the assigned chocolate for a 30 days period, after which a final evaluation was performed. Each evaluation included heart ultrasonography, carotid-femoral pulse wave velocity (PWV) and carotid pulse wave analysis (PWA), flow mediated slowing (FMS) and an analysis of the ventricular-arterial coupling (VAC).

Results: The baseline evaluation presented similar values within normal range in both groups. The positive vascular effects were overall more distinct in the group eating chocolate with the highest content in cocoa. No structural modifications on the heart were found after the intervention, notwithstanding cardiac function was improved on certain functional parameters in the HCC group only. A statistically significant improvement was depicted over the brachial and central systolic and pulse pressures in the HCC group, and a trend for improvement in the AiX and the FMS was also observed in the HCC but not in the LCC. The VAC parameters were similar at baseline between groups, but showed a significant improvement in the HCC group after intervention, increasing from 0.674 to 0.719 ($p = 0.004$), so that the post-intervention VAC was significantly higher in the HCC group compared with the LCC group ($p < 0.05$). In addition, significant variation was observed in both groups regarding arterial elastance, LV elastance, stroke work and potential energy, with greater mean differences identified in the HCC.

Conclusions: This study shows that regular consumption of HCC has beneficial effects over the cardiovascular system in young and healthy adults, improving vascular function by reducing central brachial artery pressures, promoting vascular relaxation, and enhancing VAC.

SINGLE VERSUS MULTIPLE 24-HOUR URINE COLLECTIONS FOR ESTIMATION OF LONG-TERM POTASSIUM INTAKE AND THE ASSOCIATED CARDIOVASCULAR RISK

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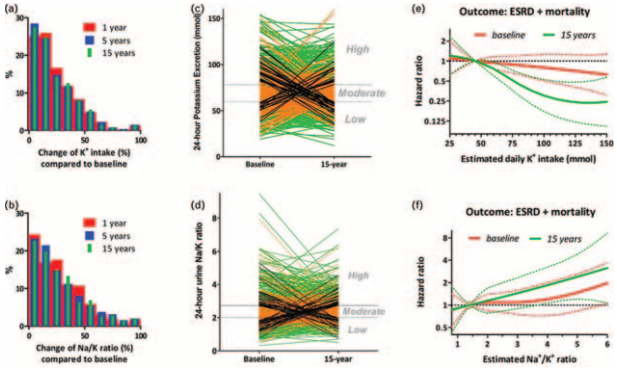
Objective: High potassium (K+) intake decreases blood pressure (BP) while high sodium (Na+) intake increases BP. Na+ and K+ intake are usually estimated with a single 24-hour urine collection. However, recent studies show that a single 24-hour urine sample is inaccurate for estimation of long-term Na+ intake. We investigated whether long-term K+ intake can be estimated with a single 24-hour urine collection, and whether urine Na+/K+ ratio may be a more stable parameter to assess electrolyte intake.

Design and method: We selected adult subjects from a tertiary hospital with an eGFR > 60 mL/min/1.73m2 who had an outpatient 24-hour urine collection between 1998–1999 and > 1 24-hour urine collection during follow-up. We estimated urine K+ excretion and Na+/K+ ratio at baseline and during 1-, 5- and 15-year follow-up. We used Cox regression analysis to assess the association between K+ excretion and Na+/K+ ratio, and cardiovascular (CV) events or mortality, and end-stage renal disease (ESRD) or mortality.

Results: We included 541 subjects aged 47 ± 14 years of whom 47% were male. We analysed 7,885 24-hour urine samples. Mean K+ excretion (74 ± 30 mmol) and mean Na+/K+ ratio (2.5 ± 1.2) were similar at baseline and follow-up. However, compared to baseline, individual K+ excretion was > 20% different in half of the subjects when using 1/5/15-year estimates (Fig A). As a result, 43–48% changed from K+ excretion tertile or urine Na+/K+ ratio tertile when estimates were based on longitudinal data instead of baseline data (Fig C-D). We recorded 113 CV events, 83 ESRD cases and 87 deaths. Although no associations between K+ excretion or Na+/K+ ratio and CV or renal outcomes were observed using baseline estimates, we observed a lower risk for ESRD with higher K+ excretion and a higher risk of ESRD with higher urine Na+/K+ ratios when estimates were based on longitudinal data (Fig E-F). Hazard ratios derived from baseline and follow-up data were up to 76% different. The inconsistency was similar for K+ excretion and Na+/K+ ratio.

Conclusions: A single 24-hour urine collection is insufficient for estimation of long-term K+ intake or urine Na+/K+ ratio and the associated CV and renal risk.



POSITIVE TRENDS IN AWARENESS OF HARMFUL EFFETCS OF HIGH SALT INTAKE - 10 YEARS CROATIAN ACTION ON SALT AND HEALTH (CRASH). DATA FROM 2008 AND 2017 WORLD HYPERTENSION DAYS

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Objective: The aim of this study was to evaluate changes in general population attitude and awareness on harmful effects of high salt consumption ten years after Croatian national action on salt and health (CRASH) was launched.

Design and method: Data on salt awareness were collected in individuals (aged 18 years or older) participating in the 2008 and 2017 World Hypertension Day in Croatia. In 2017 blood pressure (BP) was measured at 26 sites in 5 cities in Croatia from 10 AM to 2 PM in hospital open points, central squares and pharmacies. BP was measured by physicians, trained nurses, pharmacist or medical students. Along with BP measurements, a short questionnaire on hypertension awareness, salt intake and smartphone use was completed at the time of the interview. This action was organized and supported by the Croatian Society of Hypertension.

Results: A total of 2175 subjects, 873(40.1%) men, 1211(59.9%) women were examined. Awareness that increased salt intake is harmful and associated with high BP significantly increased from 2008 to 2017 (65.3% vs.95.8%);in 2017 women are more aware (91.8% vs.87.3%;p = 0.013). Comparing to 2008, in 2017, population is much more informed about harmful effects of exaggerated salt intake from physicians (48.9% vs.89.1%). In 2017 more subjects are aware that they are eating too salty than they were in 2008 (27% vs.36.1%), and more men than women thinks they are eating too salty (36.1% vs.29.8%,p = 0.02). Comparing data from 2008 and 2017 the same proportion of women believes that they would be able to reduce salt intake if suggested (86.5% vs.85.8%), but significantly more men in 2017 compared to 2008 declared that they could follow recommendations for reducing salt intake (62% vs.83.9%). Although significantly more subjects in 2017 than in 2008 are aware that bread and bakery products are the main sources of salt intake (9.5% vs.20.9%), the majority (52%) still believes that smoked meat, salami etc. is the main pathway of salt ingestion.

Conclusions: Significant improvements in awareness of harmful effects of high salt consumption were noticed in Croatia.

EFFECT OF SALT INTAKE ON PLASMA AND URINARY URIC ACID LEVELS IN CHINESE ADULTS: AN INTERVENTIONAL TRIAL

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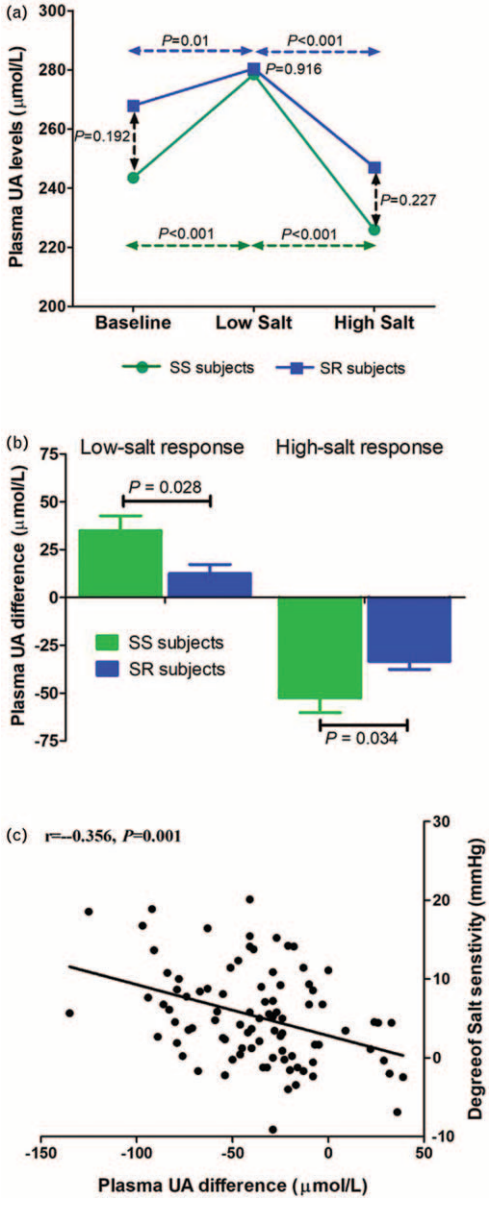
Objective: Uric acid (UA) has been proposed as an important risk factor for cardiovascular and renal morbidity. We conducted an interventional trial to assess the effects of altered salt intake on plasma and urine UA levels and the relationship between UA levels and salt sensitivity in humans.



Design and method: Ninety subjects (18–65 years old) were selected from a rural community in Northern China in our interventional study. All subjects were sequentially maintained on a normal diet for 3 days at baseline, on a low-salt diet for 7 days (3.0 g/day, NaCl), and on a high-salt diet for an additional 7 days (18.0 g/day of NaCl).

Results: Plasma UA levels significantly increased from baseline to low-salt diet (262.7 ± 7.6 vs. 280.0 ± 7.4 mmol/L, $P < 0.001$) and decreased from low-salt to high-salt diet (280.0 ± 7.4 vs. 242.6 ± 7.1 mmol/L, $P < 0.001$). By contrast, daily urinary levels of UA significantly decreased from baseline to low-salt diet (2,242.4 ± 168.3 vs. 1,558.2 ± 101.1 mmol/24 h, $P < 0.001$) and increased from low-salt to high-salt diet (1,558.2 ± 101.1 vs. 1,761.9 ± 90.2 mmol/24 h, $P = 0.032$). The 24 h urinary sodium excretions showed inverse correlation with plasma UA ($r = –0.258$, $P < 0.001$) and positive correlation with urinary UA excretions ($r = 0.176$, $P = 0.019$). Additionally, as shown in Figure, salt-sensitive subjects presented significantly higher plasma UA changes in comparison to salt-resistant subjects (low salt response: 34.9 ± 7.8 vs. 12.5 ± 4.8 mmol/L, $P = 0.028$; high salt response: -52.5 ± 7.7 vs. -33.4 ± 4.1 mmol/L, $P = 0.034$), and a negative correlation was observed between degree of salt sensitivity and plasma UA difference.

Conclusions: The present study indicates that variations in dietary salt intake affect plasma and urine UA levels, and plasma UA may be involved in the pathophysiological process of salt sensitivity.

ACUTE EFFECT OF COFFEE ON AORTIC STIFFNESS AND WAVE REFLECTIONS IN HEALTHY INDIVIDUALS: DIFFERENTIAL EFFECT ACCORDING TO HABITUAL CONSUMPTION

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Objective: Coffee and caffeine given alone acutely increase aortic stiffness and wave reflections, however, there are no studies investigating the influence of habitual vs non-habitual coffee consumption in this effect. Therefore, the present study was undertaken to investigate whether the acute effect of coffee or caffeine on aortic stiffness is different between habitual and non-habitual coffee consumers.

Design and method: The acute effect of coffee on arterial stiffness and its dependence on habitual consumption was studied in 24 volunteers on four separate occasions during which subjects received: a) coffee espresso, b) decaffeinated coffee espresso, c) caffeine alone and d) placebo (hot water).

Results: The increase in carotid femoral pulse wave velocity (PWV), augmentation index (AIx) and augmented pressure (AP) of the aortic pressure waveform after coffee consumption was more pronounced in non-habitual ($n = 13$) compared to habitual drinkers ($n = 11$), (differences of maximal changes between groups in PWV, AIx, AP responses by 0.39 m/s, 4.5% and 1.9 mmHg, respectively, for coffee; and by 0.34 m/s, 5.3% and 2.1 mmHg, respectively, for decaffeinated coffee; all $p < 0.05$).Caffeine increased PWV, as well as AIx and AP but differences in responses between the two groups were not significant.

Conclusions: Both caffeinated and decaffeinated coffee consumption is associated with a more potent effect on arterial stiffness in non-habitual than habitual coffee consumers, whereas caffeine induces comparable changes in both groups.

ORAL SESSION

ORAL SESSION 5B:
ENDOCRINE HYPERTENSION

PROSPECTIVE APPRAISAL ON THE PREVALENCE OF PRIMARY ALDOSTERONISM AND ITS SUTYPES IN HYPERTENSIVE PATIENTS PRESENTING WITH ATRIAL FLUTTER OR FIBRILLATION: PAPPHY STUDY

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Objective: Excess aldosterone has been suggested to favour and/or cause atrial fibrillation (AF), particularly in the patients with arterial hypertension, but the relationship between AF and primary aldosteronism (PA) remains uncertain. Hence, we tested the hypothesis that AF is one of the presenting signs of unrecognized PA, and investigated the prevalence of PA and its subtypes in hypertensive patients presenting with lone AF.

Design and method: Consecutive patients with an unambiguous diagnosis of arterial hypertension presenting with ECG-confirmed AF and no obvious causes of the arrhythmia were recruited and submitted to the screening and subtyping for PA according to the Endocrine Society PA current guidelines, including measurement of plasma renin activity and aldosterone levels after appropriate pharmacological preparation, and adrenal vein sampling (Funder J. JCEM 2016). The diagnosis of aldosterone-producing adenoma followed the four corner criteria, which imply cure of PA after adrenalectomy (Rossi GP. JACC 2006).

Results: From 2015 to 2017, 296 patients (age 76 ± 12 years; 48/52 F/M, %) were recruited in three ESH centers of Excellence for arterial hypertension in Italy (Padua, Brescia and Rome). Fifty-five patients, who met the inclusion criteria and had no exclusion criteria, underwent the entire diagnostic work-up for PA. This allowed to ascertain that the overall prevalence of PA was 34.5%, 42% of the cases being accounted for by aldosterone-producing adenoma and the rest by bilateral forms.

Conclusions: By providing compelling evidence for a high prevalence of PA in hypertensive patients presenting with the so-called "lone" AF, these results can lead to changing clinical practice in the management of these patients in that they indicate the need to carefully searching for PA and undertaking subtyping with the aim of pinpointing those who can be cured with unilateral laparoscopic adrenalectomy.

SENSITIVITY AND SPECIFICITY OF 24 HOURS URINARY 3-METHOXYTYRAMINES IN THE DIAGNOSIS OF MALIGNANT PHEOCHROMOCYTOMA AND PARAGANGLIOMA

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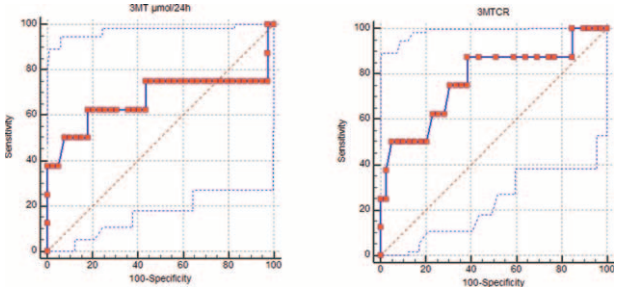
Objective: At least 10% of pheochromocytoma and sympathetic paraganglioma (PPGL) are malignant, yet there is no specific biomarker of malignancy. Societies guidelines sugget the use of 3 Methoxytyramines (3MTT) for the diagnosis of malignancy, however few studies evaluated 24H-urinary 3MTT as a predictor of malignancy. The aim of this study was to evaluate the sensitivity/specificity of 24H-Urinary 3MTT for the diagnosis of malignant PPGL



Design and method: We conducted a retrospective study of electronic registers of Hypertension excellence center of Georges Pompidou hospital, from 2012 to 2015 to identify patients who completed PPGL-workup: Measurement of 24H-Urinary metanephrines/Normetanephrines(MTN/NMT) and 24H-Ur 3MTT by LCMS, Imaging exams to confirm/exclude PPGL, histopathological diagnosis of PPGL after surgery. We excluded from our analysis patients without the diagnosis of PPGL, under medications interacting with MTN/NMT/3MTT secretion, or without 24H-Ur 3MTT determination Determination of 24H-Ur MTN/NMT/3MTT was made by LCMS method with validated protocol. We first analysed ROC parameters for 24h-Ur 3MTT, then those of 24H-Ur 3MTT to 24H-Ur creatinine ratio.

Results: 47 patients were included in this study:8 malignant PPGL and 39 non malignant PPGL. ROC curve of sensitivity(1-specificity) of 24h-Ur 3MTT for the diagnosis of PPGL malignancy showed an area under curve(AUC) of 0.671[95%CI 0.519–0.801]: The optimal criterion of the curve corresponded to a value of 24h-Ur 3MTT of 4.67 mmol/24 h and showed a specificity of 82.05% and sensitivity of 62.5% for malignancy diagnosis. A value > 12 mmol/24 h of 24h-Ur 3MTT offered 100% specificity with 37.5% of sensitivity ROC curve of sensitivity(1-specificity) of 24h-Ur 3MTT/24h-Ur Creatininuria for the diagnosis of PPGL malignancy showed an AUC of 0.774 [95%CI 0.629–0.883]: The optimal criterion of the curve was 1.25 mmol/mmol with a specificity of 94.87% and a sensitivity of 50% for the diagnosis of malignancy. A value of 24h-Ur 3MTT/Cr > 1.73 mmol/mmol offered 100% specificity with 25% sensitivity.

Conclusions: These data sugget that 24h-Urinary 3MTT measured by LCMS and 24h-Ur 3MTT to creatinine ratio could be used as valuable biomarkers for the diagnosis of malignant PPGL. Values superior to 4.67 mmol/l and 1.25 mmol/mmol respectively offered the best compromise between high specificities and average sensitivities.

RAAS TRIPLE A-TESTING: COMBINING LC-MS/MS BASED MOLECULAR PROFILING OF HYPERTENSION AND ADVANCED SCREENING FOR PRIMARY ALDOSTERONISM

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Objective: RAAS Triple-A testing is a novel mass spectrometry based approach providing a comprehensive biochemical evaluation of the circulating renin-angiotensin-system (RAS) on the basis of equilibrium angiotensin levels and circulating aldosterone levels.

Design and method: In contrast to previous technologies involving complex sampling procedures, RAS-Equilibrium-Analysis combines the robustness and accuracy of LC-MS/MS based quantification with the versatility of serum sampling to generate a highly accurate readout containing multiple layers of information regarding the biochemical features of the circulating RAAS. Equilibrium Angiotensin I (Ang I), Angiotensin II (Ang II) and Aldosterone were simultaneously quantified in 500 microL of standard collected serum samples from healthy volunteers or hypertensive patients receiving different anti-hypertensive first-line therapies. Stable-isotope labeled internal standards were used to control for analyte recovery. Following analyte extraction, samples were subjected to UPLC-MS/MS analysis and diagnostic ratios were calculated.

Results: ACE inhibitor therapy resulted in a significant reduction of the Ang II-to-Ang I-Ratio in equilibrium analysis, which was accompanied by an up-regulation of renin, as expected. Surprisingly, PRA showed a high correlation with the sum of equilibrium Ang I and Ang II, which was independent of ACE inhibitor treatment. While the ARR was strongly suppressed in the presence of ACE inhibitor treatment, the Aldosterone-to-Angiotensin II-Ratio (AA2-Ratio) was not affected, suggesting superior applicability in screening for primary aldosteronism (PA).

Conclusions: Triple-A testing is a mass spectrometry based multiplex assay combining Ang I, Ang II and Aldosterone to diagnostic values that draw a comprehensive picture of a patient's RAAS Status. While the sum of Ang I and Ang II serves as a strong PRA surrogate marker, ACE activity and ACE inhibitor therapy efficacy can be monitored using the Ang II/Ang I-Ratio. On top, the AA2-Ratio serves as an advanced diagnostic marker for PA that might pave the way for patient screening without the need of withdrawing anti-hypertensive therapies.

CARDIOVASCULAR EVENTS AND TARGET ORGAN DAMAGE IN PRIMARY ALDOSTERONISM: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: According to some reports, patients affected by primary aldosteronism (PA) have an increased risk of cardio- and cerebrovascular complications compared to patients with essential hypertension (EH). However, current available evidence relies on highly heterogeneous studies.
We aimed to assess the relationship between PA and major adverse cardiac and cerebrovascular events, cardiac target organ damage, diabetes and metabolic syndrome by integrating results of previous studies.

Design and method: We performed a meta-analysis of both prospective and retrospective observational studies to investigate the association between PA and stroke, coronary artery disease (as co-primary end points), atrial fibrillation and heart failure (as secondary endpoints), target organ damage, metabolic syndrome and diabetes, in comparison with patients affected by essential hypertension. We also compared PA subtypes, aldosterone producing adenoma (APA) and bilateral adrenal hyperplasia (BAH).

Results: A total of 31 studies, including 3838 patients with primary aldosteronism and 9284 patients with essential hypertension were included in the analysis. After a median of 8.8 years from hypertension diagnosis, compared with patients with essential hypertension, patients with primary aldosteronism displayed an increased risk of stroke (odds ratio [OR] 2.58, 95% CI 1.93–3.45), coronary artery disease (1.77, 1.10–2.83), atrial fibrillation (3.52, 2.06–5.99), and heart failure (2.05, 1.11–3.78). Similarly, the risk of diabetes (OR 1.33, 95% CI 1.01–1.74), metabolic syndrome (1·53, 1·22–1·91), and left ventricular hypertrophy (2.29, 1.65–3.17) was increased in patients affected by PA compared with EH.

Conclusions: An early diagnosis of PA is important because affected patients display an enhanced cardiovascular risk compared to patients with EH.

SEATED SALINE SUPPRESSION TESTING FOR THE DIAGNOSIS OF PRIMARY ALDOSTERONISM. A VALIDATION STUDY

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Objective: Primary aldosteronism (PA) is confirmed by failure of plasma aldosterone (aldo) suppression during fludrocortisone (FST) or saline suppression testing (SST). Aldo can be higher upright (e.g. seated) than recumbent in PA; upright levels are used during FST. We hypothesized that seated SST (SSST) is more sensitive than recumbent (RSST). In our pilot study of 24 patients with confirmed PA, 23 tested positive by SSST compared to 8 by RSST (JCEM2014;99:2745–53). The current validation study involved 100 patients who underwent FST, RSST and SSST, eight of them both before and after unilateral adrenalectomy. Of the 108 FSTs, 94 were performed on hypertensives with raised aldo/renin ratios to confirm/exclude suspected PA (PreADX), and 14 on patients following adrenalectomy for previously diagnosed unilateral PA to confirm/exclude cure (PostADX). For SSTs, aldo was measured basally at 8am and after 2 L normal saline infused over 4 h in either the seated or recumbent position.
Of the 108 FSTs, 73 confirmed PA, 17 excluded PA and 18 were inconclusive. Four patients with inconclusive FST lateralized on adrenal venous sampling (confirming unilateral PA), making a total of 77 with PA. Among the 84 patients with conclusive FST, SSST and RSST results, ROC analysis established optimal cut-off aldo levels of 163 pmol/L for SSST and 105 pmol/L for RSST. At these cut-offs, SSST showed much greater sensitivity than RSST (87 vs 41%; $p = 0.012$) but similar specificity (94 vs 100%; NS). The area under the ROC curve was greater for SSST than RSST (0.96 ± 0.02 SE vs 0.81 ± 0.06; $p < 0.01$). Of 28 patients with unilateral PA, 26 (93%) were positive, one negative and one inconclusive by SSST, while 20 (71%) were positive, six negative and two inconclusive by RSST. Of 43 with bilateral PA, 36 (84%) were positive, six negative and one inconclusive by SSST, while only 8 (19%) were positive, 32 negative and three inconclusive by RSST. Of 17 with PA excluded by negative FST, 16 (94%) were negative and one positive by SSST and 16 (94%) were negative and one inconclusive by RSST. Among the entire set of 108 studies performed, only three SSST (vs 9 RSST and 18 FST) results were inconclusive.
SSST is much more sensitive than RSST, has a similar low false positive rate, and has a lower proportion of inconclusive results than either RSST or FST. It therefore offers a reliable and much less complicated and expensive alternative to FST for the confirmation of PA.

PREVALENCE OF THE MAIN FORMS OF LOW RENIN HYPERTENSION: A RETROSPECTIVE, SINGLE CENTER STUDY

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Objective: Hypertensive patients can be classified to low, normal or high-renin hypertension based on their plasma renin activity (PRA) levels. Low renin hypertension (LRH) is characterized by suppressed renin with low, normal or high level of plasma aldosterone, which can be further identified as low renin essential hypertension (LREH), primary aldosteronism (PA) and a small number of genetic subtypes in young patients by specific confirmatory tests. The aim of this retrospective study was to investigate the prevalence of the main forms of LRH.

Design and method: This is a retrospective, single center study. Consecutive adult inpatients of Hypertension Center of People's Hospital of Xinjiang Uygur Autonomous Region from January 2008 to December 2010 were studied. 1275 hypertensive subjects were measured seated plasma renin activity (PRA) and plasma aldosterone concentration (PAC) after washing out influential drugs and correcting hypokalemia, finally, 769 subjects were defined as LRH (PRA < 1.0ng/ml/h). The positive screening test for PA was based on aldosterone/renin ratio (ARR) > 20 (ng/dl)/(ng/ml/h) and the diagnosis of PA was based on saline infusion test (SIT) criteria in accordance with the Endocrine Society Guideline. Subjects with post-SIT PAC > 10 ng/dl were labeled as "overt PA", those with post-SIT PAC between 5 and 10 ng/dl were labeled as 'milder PA', and those with post-SIT PAC < 5 ng/dl or ARR < 20 were considered to be LREH.

Results: The prevalence of LREH, 'milder PA' and 'Overt PA' was 42.1%, 36.8% and 21.1% in the whole LRH, respectively. The prevalence of PA (including milder and overt PA) in LRH was 57.9%.

Conclusions: Our data show that PA (including milder and overt PA) is the main form of LRH, while LREH and milder form of PA are more common than overt PA in LRH.

ALDOSTERONE INDUCES CYP11B2 GENE EXPRESSION VIA GPER-1 ACTIVATION IN HUMAN ADRENOCORTICAL CELL (HAC15) AND STRIPS FROM ALDOSTERONE PRODUCING ADENOMA

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Objective: We previously reported that GPER-1 is mostly expressed in the zona glomerulosa of normal human adrenal gland and in aldosterone-producing adenoma (APA). In the adrenocortical carcinoma cell line HAC15 17b-estradiol induces aldosterone synthesis via GPER-1 activation. Since GPER-1 was found to bind not only 17b-estradiol, but also aldosterone in endothelial and vascular smooth muscle cells, we wondered if aldosterone binds GPER-1 receptor also in the adrenocortical cells, thereby modulating its own synthesis.

Design and method: APA strips and adrenocortical carcinoma cell line HAC15 were exposed to [100 nM] aldosterone for 12 hours in the presence or absence of the selective mineralocorticoid receptor (MR) antagonist canrenone and/or of the selective GPER-1 antagonist G36. HAC15 cells were silenced for GPER-1 with specific small interfering RNA (siRNA) and then exposed to aldosterone. The changes of aldosterone synthase (CYP11B2) mRNA and protein levels were measured by real time qRT-PCR and immunoblotting.

Results: Aldosterone increased CYP11B2 gene and protein expression (+200% and +130%, respectively) in HAC15 cells ($p < 0.001$ vs untreated). Pretreatment with canrenone did not prevent such increase, while G36 abolished aldosterone-induced CYP11B2 activation ($p < 0.01$). In APA strips aldosterone increased CYP11B2 gene expression (+330%, $p < 0.01$ vs untreated); pre-treatment with G36 blunted this effect of aldosterone. Silencing of GPER-1 with siRNA not only reduced GPER-1 expression ($p < 0.01$), but also abolished the CYP11B2 increase in response to aldosterone.

Conclusions: Aldosterone enhances the expression of CYP11B2 acting via GPER-1, but not MR. Binding of aldosterone to GPER-1 could contribute to perpetuating the autonomous aldosterone excess, which is a hallmark of primary aldosteronism, via an autocrine-paracrine positive feed-back loop.

ADRENAL VENOUS SAMPLING: THE GOLD-STANDARD FOR SURGICAL INDICATION IN PRIMARY ALDOSTERONISM

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Objective: An increasing incidence of primary aldosteronism among the main causes of secondary arterial hypertension has been described elsewhere. If surgical indication is correct, the chances of complete curation of blood pressure rising will be quite elevated. Incorrect surgical indication correlates to a clinical failure.

Aims: To show that the aldosterone adrenal veins sampling is indispensable in order to indicate surgical treatment in primary aldosteronism.

Design and method: Primary aldosteronism diagnosis was confirmed in 185 patients as their plasmatic renin-to-aldosterone ratio was equal or higher than 30. Computerized tomography (CT) was performed in 159 and scintigraphy in 86. Selective adrenal venous sampling was completed in 81 patients. Diagnostic efficacy to classify the type of primary aldosteronism by CT, scintigraphy and selective adrenal sampling has been evaluated by comparing the findings in image test and results of aldosterone and cortisol adrenal sampling.

Results: Confirmation of the radiological adenoma by CT was possible in only 16 out of 81 patients after venography performance (19,75%). After completion of the study, therapeutic attitude was modified in 32 patients (40%) after showing bilateral aldosterone hypersecretion though unilateral pathological imaging by CT. Among the remaining patients, adrenal sampling was interpreted as unilateral alteration more than bilateral as CT had stated. Venography results were corresponding with CT in 18 cases for diagnosis other than adenoma.
In summary, venography results were coincident with morphologic imaging in 40%. A weak concordance index has been obtained (kappa = 0,253) between CT-guided diagnosis and final diagnosis by venography. Cocordance index for scintigraphy was also poor (kappa = 0,066).

Conclusions: Selective adrenal venous sampling must be performed in order to examine plasmatic aldosterone and cortisol levels to accurate classification and the definite treatment of primary aldosteronism, especially a surgical indication.

URINARY POTASSIUM LOSS INDUCED BY HYPERALDOSTERONE SECRETION ASSOCIATED WITH DIABETES MELLITUS PREVALENCE IN HYPERTENSIVE PATIENTS

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Objective: Primary aldosteronism(PA) is characterized by hypersecretion of aldosterone with increased urinary potassium(K+) excretion and hypertension. Diabetes was more frequent in PA and the association between DM and PA involved in hypokalemia. The status of low serum K+ was related to chronic urinary K+ excretion. The aim of this study was to find out whether hyperaldosterone and urinary K+ excretion could increase the risk of diabetes in patients with PA.

Design and method: 790 hypertensive in-patients were enrolled from Hypertension Center of People's Hospital Of Xinjiang. DM participants included patients with known or newly-diagnosed diabetes. All of them entered a protocol for screening PA. The positive initial screening group was defined on plasma aldosterone concentration (PAC) /renin activity (ARR) > 20 ng/dL per ng/mL/h. PA group was according on ARR > 20 plus PAC > 10 ng/dL after saline infusion test. Baseline characteristics were collected including blood pressure, lipids, plasma renin activity, PAC, serum K+ and 24 h-urine K+ levels. The relationship of hyperaldosterone or urinary K+ excretion with DM was evaluated during the screening process of PA.

Results: In positive screening group, 24 h-urine K+ levels or PAC associated with DM prevalence, age tertile (OR 3.173, 95%CI 1.801–5.590, $p < 0.01$), urinary K+ tertile(OR 2.221, 95%CI 1.251–3.942, $p < 0.01$), PAC tertile(OR 1.728, 95%CI 1.091–2.737, $p < 0.05$) and the cumulative contribution(OR 1.262, 95%CI 1.073–1.483, $p < 0.01$), independent of systolic blood pressure and lipids. Compared with 86 age- and sex-matched patients without PA, patients with PA had significantly higher PAC (22.3+11.9 vs 12.6+5.7, $p < 0.01$), lower 24 h-urine K+ levels (46.2+29.9 vs 35.9+15.2, $P < 0.01$), and higher DM prevalence (29.1% vs 9.3%, $P < 0.01$). The level of urinary K+ (52.5+17.0 vs 46.7+21.3 vs 35.7+17.7, $P < 0.05$) and PAC (22.4+9.9 vs 22.9+17.2 vs 12.8+5.53, $p < 0.05$) were different significantly among three groups with PA&DM, single PA and no-(PA&DM) match for -age and -sex in a 1:1:1 fashion. And the correlation of 24 h-urine K+ levels or PAC with DM prevalence was clear among the groups, the coefficient of correlation were 0.323 and 0.300, respectively($P < 0.01$).

Conclusions: Urinary potassium loss induced by hypersecretion of aldosterone associated with DM prevalence in patients with hypertension.

ORAL SESSION

LATE-BREAKERS:
SESSION 2

PERFORMANCE OF THE AAP 2017 GUIDELINE SIMPLE TABLE ON BP SCHOOL-BASED SCREENING IN A EUROPEAN POPULATION

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Objective: We assessed the performance on BP population screening of the simplified AAP 2017 clinical practice guideline based on age and 5th percentile of height, and a similar simplified table based on the 4th Report BP reference tables compared to the ESH 2016 guideline diagnostic thresholds.

Design and method: We obtained data from a school-based screening study for the prevalence of high BP in the municipality of Kastoria in north Greece. Blood pressure was measured thrice by a mercury sphygmomanometer according to ESH 2016 guidelines and the last two BPs were averaged for the analysis.

Results: The study population included 1,846 children aged 6–12 years and 986 adolescents aged 13–18 years. Compared to the ESH 2016 classification, the AAP 2017 table showed AUC 0.936, sensitivity 95.5%, specificity 91.6%, NPV 99.8%, and PPV 36%, while the 4th report table showed AUC 0.963, sensitivity 99.2%, specificity 93.3%, NPV 100%, and PPV 42.2%. The performance of the 4th report table was similar in both age groups, while the performance of the AAP 2017 table was lower in the adolescent group (AUC 0.884, sensitivity 83.2%, specificity 93.5%, NPV 99.3%, and PPV 32.6%, in adolescents versus AUC 0.953, sensitivity 100%, specificity 90.6%, NPV 100%, and PPV 37.2% in 6–12 years-olds, $P < 0.05$ for difference in AUC between age groups). Comparing the prevalence of elevated BP by the two simple tables we found agreement by both tables in 96.9% of the subjects (86.7% had normotension and 10.2% had high-normal or hypertensive BP levels), and disagreement in 3.1%. All children classified for further screening by AAP 2017 table were normotensive by ESH 2016 classification. However, 20,8% of the adolescents classified for further screening by 4th report, but not by AAP 2017 table, had BP levels at the high-normal category according to ESH 2016 classification.

Conclusions: Simple tables for BP screening based on age present good performance to identify children and adolescents with normal BP levels. However, the table by AAP 2017 guideline may provide high rate of false positive results and fail to classify adolescents eligible for further BP measurements and lifestyle modification.

DIFFERENCES IN THE PREVALENCE OF BLOOD PRESSURE CONDITIONS USING ESH VS AAP GUIDELINES IN CHILDREN AND ADOLESCENTS

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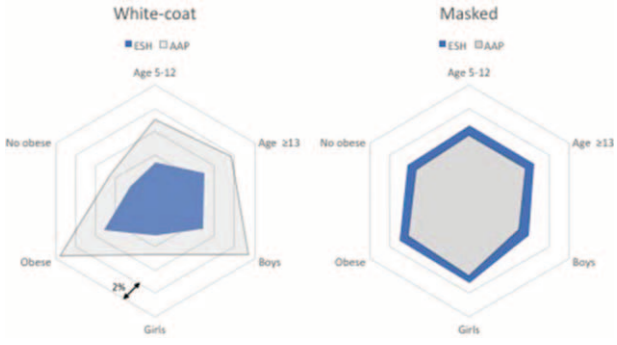
Objective: The objective is to assess differences in the prevalence of blood pressure (BP) conditions according to the European Society of Hypertension (ESH) guidelines (Lurbe, J Hypertens 2016) and the American Academy of Pediatrics (AAP) (Flynn, Pediatrics 2017) in children and adolescents.

Design and method: Four thousand two hundred and ninety-six Caucasians of both sexes (1941 females), of European origin, from 5 to 18 years of age (mean age 11.5 3.3) in the absence of antihypertensive treatment were included. Overweight and obesity (n = 2243) were defined based on the extended international body mass index cut-offs. Office BP was measured in the non-dominant arm with cuff and bladder size adjusted to upper-arm girth. The three measurements of each office visit were averaged for analysis. Twenty-four-hour ambulatory BP monitoring was performed by using Spacelabs monitor 90207. Subjects were qualified as true normotensive (N), white-coat (WC), masked (M) or sustained hypertensive (HTN) according to the ESH and AAP criteria for office BP, and reference values for 24-hour ambulatory BP (Wühl, J Hypertens 2002).

Results: The prevalence of N, WC, M and HTN were significantly different when the ESH or AAP were applied. Overall, the largest differences were observed in the prevalence of WC, which was double when the AAP criteria were used. The differences were larger for boys, older than 13 years of age. The presence of obesity did not reduce the higher prevalence of WC by the AAP criteria. In contrast, M was slightly higher when the ESH criteria were applied. The impact on the prevalence of WC and M is shown in the figure.



Conclusions: When applying the AAP criteria, compared with that of the ESH, the main difference is the higher prevalence of WC, especially in boys aged 13 years or older. The consequence is an increment of the HTN work-up in children and adolescents.

POTENTIAL IMPACT OF THE 2017 ACC/AHA HIGH BLOOD PRESSURE GUIDELINE IN NORMOTENSIVE PATIENTS WITH STABLE CORONARY ARTERY DISEASE: INSIGHTS FROM THE CLARIFY REGISTRY

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Objective: The 2017ACC/AHA high blood pressure (BP) guideline lowered the threshold defining hypertension and BP target in high-risk patients to 130/80 mmHg, Patients with coronary artery disease (CAD) and systolic BP 130–139 mmHg or diastolic BP 80–89 mmHg should now receive medication to achieve this target. We aimed to investigate the relationship between BP and cardiovascular events in "real-life" CAD patients considered as normotensive until the recent guideline.

Design and method: Data from patients with stable CAD, with no history of hypertension and baseline BP < 140/90 mmHg, receiving > = 1 BP-lowering medication prescribed for angina, enrolled in the international CLARIFY registry from November 2009 to June 2010, were analyzed. Patients with heart failure were excluded. A Cox proportional hazards model was used to evaluate the relationship between average BP during follow-up and cardiovascular outcomes. SBP subgroups were defined as < 120 mmHg, 120–129 mmHg (reference), 130–139 mmHg, and > = 140 mmHg. DBP subgroups were defined as < 60, 60–69 mmHg, 70–79 mmHg (reference), 80–89 mmHg, and > = 90mmHg. The primary endpoint was the composite of cardiovascular death, myocardial infarction and stroke, and secondary endpoints were each component of the primary endpoint.

Results: In 5826 patients (median follow-up 5.0 years), diastolic BP 80–89 mmHg, but not systolic BP 130–139 mmHg, was associated with an increased risk of the primary

endpoint (adjusted HRs 1.81, 95% CI 1.09–2.99, and 0.80, 95%CI 0.46–1.40, versus 70–79 mmHg and 120–129 mmHg, respectively). Similar results were observed for cardiovascular death and stroke. No significantly increased risk was observed for systolic BP < 120mmHg for either endpoint (HR 1.26, 95% CI 0.76 - 2.07, for the primary endpoint). Diastolic BP < 70mmHg was associated with an increased risk of the primary outcome, but the same was observed for stroke, suggesting a degree of reverse causality.

Conclusions: In this population of stable CAD patients defined as normotensive according to the 140/90 mmHg threshold, and receiving antianginal BP-lowering medication, achieved diastolic BP 80–89 mmHg was associated with increased cardiovascular risk while achieved systolic BP 130–139 mmHg was not, supporting the lower diastolic but the not the lower systolic BP hypertension-defining threshold and treatment target.

COMPARATIVE EFFECTIVENESS OF TWO-DRUG THERAPY VERSUS MONOTHERAPY AS INITIAL REGIMEN IN HYPERTENSION: A PROPENSITY-SCORE MATCHED COHORT STUDY IN A LARGE PRIMARY CARE DATABASE

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Objective: Clinical trials have shown initial combination therapy to be more effective on blood pressure (BP) control than initial monotherapy but few studies examined the question in a large primary care database. The main objective of this study was to evaluate relative effectiveness on BP of an initial two-drug therapy compared to monotherapy in hypertension (HT).

Design and method: In the UK Clinical Practice Research Datalink with hospitalisation and mortality data linkage, we identified a cohort of adults with uncontrolled HT and initiating one or two antihypertensive drug class(es) (among ACEIs, ARBs, CCB, BB, thiazide-like diuretics) between 2006 and 2014, with follow-up until February 2016. New users of 2-drugs and monotherapy were matched 1:2 using a propensity score. Exposure was defined as intention-to-treat (ITT) or as treated (AT), i.e. until first regimen change. Primary and secondary endpoints were respectively BP control and serious cardiovascular event (SCE). Analyses in planned subgroups, according to HT severity or most frequent classes of drugs (ACEi, CCB) used specific propensity scores.

Results: Among 54,523 eligible hypertensive patients included, 3,256 patients were initiated on 2 drugs of which 2,807 (86.2%) were matched to 5,614 monotherapy new users (mean SBP/DBP 164.6/94.8 mm Hg). During a mean follow-up (ITT) of 4.6 years, mean exposure duration (AT) was 12.7 months, with 76.5% patients changing initial regimen. In the AT analysis, use of 2 drugs was associated with 17% increased BP control in all hypertensive patients (HR [95%CI]: 1.17 [1.09–1.26]), increasing to 28% in patients with grade 2–3 HT (1.28 [1.17–1.41]), and 27% in patients with ACEi+CCB (1.27 [1.08–1.49]). A positive association was also observed in the ITT analysis of all hypertensive patients (1.08 [1.03–1.13]) or those with grade 2–3 HT (1.10 [1.03–1.18]). For SCE, overall no significant association with 2-drug therapy was found.

Conclusions: In line with UK guidelines, only a small fraction of hypertensive patients used two drugs in combination as initial therapy. This large population-based cohort study supports the evidence of greater effectiveness of 2-drug therapy for BP control, while additional data would be required for SCE.

INTERVENTIONS TO IMPROVE CONTROL OF HYPERTENSION; WHAT WORKS (AND WHAT DOESN'T)?

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Objective: In undertaking a Cochrane systematic review of allied health professional-led interventions for hypertension, we found greater blood pressure (BP) lowering and BP target achievement with both nurse-led and pharmacist-led care, in comparison to usual (doctor-led) care. We identified elements of these complex interventions associated with successful outcomes. Here we present further analyses to describe key components of effective BP lowering interventions.

Design and method: Univariable and multivariable meta-regression: study level descriptive variables for populations (setting, ethnicity, co-morbidity) and interventions (duration, review frequency and method, medication management, and BP target) were tested against change in systolic BP and achievement of study BP targets. Where univariable analyses suggested an association ($P < 0.1$) variables were included in multivariable models. The final model informed a hierarchical classification of interventions to compare effectiveness between groups.
Scientific Data Searches to July 2017 identified 1618 unique citations; 398 full texts were reviewed and 120 randomised controlled trials contributed data to the meta-regression dataset.

Results: Reduction in systolic BP was negatively associated with telephone delivery of interventions ($P = 0.02$). A multivariable model including three factors: face to face delivery of care, frequency of intervention, and ability to change medication, accounted for one third of variance between studies ($R2 = 34\%$). Hierarchical classification of studies based on these three elements predicted increasing magnitude of BP reduction ($P < 0.001$). Achievement of study BP targets was associated with both duration of interventions and the systolic BP target set ($R2 = 14\%$). Relative risk for achievement of study targets declined as systolic BP targets were lowered, with evidence for effectiveness down to a target of 130mmHg.

Conclusions: Effective interventions to lower blood pressure require face to face contact. Telephone support or substitution appears ineffective. Ability to change medication is a key component of successful interventions, and review should take place at least monthly until BP is at target. Interventions are shown to be effective for systolic targets of 130mmHg or higher, and are sensitive to duration of the intervention. These findings should inform future studies and guidelines.

A COMPARISON BETWEEN USUAL OFFICE AND FOUR OTHER METHODS TO EVALUATE BLOOD PRESSURE (BP-TRUE, HBPM, ABPM AND CBP) DURING 3 YEARS FOLLOW-UP

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Objective: Recently the methodology used to estimate blood pressure (BP) in the SPRINT study (3 measurements with an OMRON device with the patient isolated) has questioned the applicability of a goal of systolic BP below 120 mmHg. We have compared differences between 5 methods of BP measurements.

Design and method: A total 615 patients with pre-diabetes (N = 431) and type 2 diabetes (N = 184) were included in the study. Office BP was estimated through 3 observed measurements. The other methods were: BP-TRUE (N = 184), HBPM (N = 431), ABPM (N = 615) and CBP (N = 615) used under the standard conditions. Patients were followed for 3 years during which serum creatinine, pulse wave velocity (PWV), and other biochemical parameters were analyzed

Results: Office BP exhibited the highest and CBP the lowest values. At the end of follow-up, Office BP was 133 in pre-diabetic and 135 mmHg in diabetic patients that were 3 and 15 mmHg above at baseline. The Table shows the differences between methods in prediabetic and diabetic patients. A subtle but continuous rise was observed in serum creatinine and PWV during the follow-up of diabetics.

Table. Differences between office systolic BP and the other methodologies in prediabetic and diabetic patients.

	Baseline	3-Years
PREDIABETIC		
HBPM	3.91 (3.16-4.66)	3.53 (1.86-5.20)
ABPM	8.89 (7.84-9.87)	8.70 (6.71-10.68)
CBP	11.69 (11.15-12.23)	12.53 (11.18-13.88)
DIABETIC		
BP-TRUE	4.29 (3.23-5.34)	4.60 (3.40-5.80)
ABPM	13.44 (10.19-16.69)	5.00 (-0.10-10.10)
CBP	16.05 (13.20-18.90)	9.99 (5.50-14.47)

Conclusions: The 5 methods compared require the consideration of different BP goals to attain the maximal benefit of BP reduction. The best approach compared to office BP corresponds to ABPM and CBP followed by HBPM and BP-TRUE. Cardiorenal disease progresses in established diabetics with an acceptable BP control.