Featured Posters – Blood Pressure Measurement/ Monitoring

FP-1

AMBULATORY BLOOD PRESSURE MONITORING AND CARDIOVASCULAR EVENTS IN HIGH-RISK PATIENTS

Alejandro de la Sierra†,[1] Julian Segura,[2] Jose R. Banegas,[2] Manuel Gorostidi,[2] Felipe Madruga,[2] Xavier Clar,[2] Teresa Gijon,[2] Luis M. Ruilope[2]. [1]Hospital Mutua Terrassa, Terrassa, Spain and [2]Spanish Society of Hypertension, Madrid, Spain.

Background and Aim: Ambulatory BP (ABP) is probably a better predictor of cardiovascular events (CE) than office BP (OBP), although its role in treated hypertensives in real life conditions is less known. The Cardiorisc Event study aimed to evaluate the association of ABP with the development of CE in high-risk patients included in the Spanish ABPM Registry.

Methods: A total of 2115 hypertensive patients with either three or more additional risk factors, diabetes, documented target organ damage or previous cardiovascualr or renal disease were included. They entered the Spanish ABPM Registry between 2005 and 2006. Vital status and the development of CE were checked during 2009. The primary combined endpoint was the sum of death from cardiovascular causes, non-fatal myocardial infarction, non-fatal stroke and coronary or peripheral revascularization procedures.

Results: They were 268 primary events. The relationship between ABP values and the appearance of cardiovascular events is detailed in the Table.

Conclusion: After adjustment for OBP and cardiovascular risk factors and diseases, ABP is related with the development of CE. Systolic and pulse pressures measured 24-hour, daytime and nighttime, all show positive correlations. In the case of diastolic BP, this relationship is only observed with nighttime values. A high night/day ratio is also associated with a higher risk for cardiovascular events.

Table. Differences in BP between patients with and without cardiovascular events

Parameter	With CV event	Without CV event	Unadjusted *P*	Adjusted by OBP*	Adjusted by OBP and confounders**
24-hour SBP	136.0 ± 18.0	130.7 ± 15.3	<0.001	<0.001	<0.001
24-hour DBP	72.8 ± 10.7	73.8 ± 9.9	0.154	0.130	0.119
24-hour PP	63.2 ± 14.8	57.0 ± 12.7	<0.001	<0.001	<0.001
Day time SBP	137.3 ± 18.1	133.4 ± 15.6	0.001	<0.001	0.002
Day time DBP	74.6 ± 11.1	76.3 ± 10.4	0.015	0.730	0.471
Day time PP	62.8 ± 14.9	57.1 ± 13.0	<0.001	<0.001	<0.001
Nighttime SBP	132.1 ± 20.5	123.5 ± 17.2	<0.001	<0.001	<0.001
Nighttime DBP	68.1 ± 11.6	66.9 ± 10.4	0.123	<0.001	0.001
Nighttime PP	64.0 ± 15.7	56.6 ± 13.2	<0.001	<0.001	<0.001
SBP Night/ Day ratio	0.96 ± 0.09	0.92 ± 0.9	<0.001	<0.001	<0.001
DBP Night/ Day ratio	0.92 ± 0.10	0.88 ± 0.09	<0.001	<0.001	<0.001

*Office SBP, DBP or PP depending on the ABP checked. ** Age, gender, diabetes status, and previous CV or renal disease.

Keywords: Ambulatory blood pressure monitoring; Cardiovascular events

FP-2

A PERFECT REPLACEMENT FOR THE MERCURY SPHYGMOMANOMETER: THE CASE OF THE HYBRID BLOOD PRESSURE MONITOR

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The mercury sphygmomanometer is regarded as the most accurate device for blood pressure (BP) measurement against which new devices should be validated. However, for environmental reasons mercury devices are progressively banned. This study validated a hybrid mercury-free auscultatory device (Nissei DM3000) aiming to replace the mercury sphygmomanometer for office use and also as a standard for the validation of new devices. The tested device was validated using the European Society of Hypertension International Protocol (ESH-IP) 2010 with simultaneous BP measurements and increased number of BP comparisons. Thirty-three subjects fulfilling the ESH-IP requirements had 6 BP measurements taken simultaneously by a supervisor (S) using the tested device and 2 observers (A and B) using mercury sphygmomanometers (198 readings). The ESH-IP analysis based on 99 BP readings showed: mean device-observer systolic/diastolic BP difference 0.2 ± 2.0/0.1 ± 2.0 mmHg; systolic BP differences ≤5/10/15 mmHg in 97/99/99 readings respectively and diastolic 98/99/99; all 33 subjects with 2 of 3 BP differences ≤5 mmHg and none without a difference ≤5 mmHg (systolic and diastolic). Further analysis based on 198 BP readings showed: mean differences S-A 0.1 ± 2.4/0.2 ± 2.4 mmHg (systolic/diastolic), S-B 0.3 ± 2.1/ 0.2 ± 2.2, A-B 0.2 ± 2.4/0.0 ± 2.3; Differences ≤2 mmHg S-A in 88/84% (systolic/diastolic), S-B 87/85%, A-B 87/86% and ≤4 mmHg S-A 95/96%, S-B 95/96%, A-B 95/98%. These data suggest that a hybrid mercury-free auscultatory BP monitor comfortably passed the ESH-IP 2010 validation requirements for clinical use and has the same level of accuracy as the mercury sphygmomanometer. This device appears to be a reliable alternative to the mercury sphygmomanometer for office use and also as a standard for future validation studies of new BP devices.

Keywords: Validation; Mercury sphygmomanometer; Office blood presure measurement; International protocol

FP-3

IMPROVEMENT IN BLOOD PRESSURE CONTROL AMONG HYPERTENSIVE PATIENTS TREATED IN THE DEPARTMENT OF VETERANS AFFAIRS

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Despite the demonstrated benefits of blood pressure treatment and control, hypertension control rates remain low worldwide. Improving control blood pressure control has become a top priority for many institutions and health care organizations. The Veterans Affairs (VA) electronic health record (EHR).

We assessed improvement in control rates in 478,191 hypertensive patients treated in 15 VA Medical Centers across the US. All blood pressure readings were recorded starting in 2000. Hypertensives were those patients with elevated readings on three separate days, plus at least 1 reading following the 3rd elevated day. Only readings after the 3rd elevated are analyzed here. The last daily reading of each calendar month was saved for September 2000 through August 2010. Mean yearly increase was calculated by taking the

mean difference between the same months in adjacent years, for example (Aug/2001–Aug/2000), (Sep/2001–Sep/2000, (Oct/2001–Oct/2000), etc. All blood pressure (BP) readings recorded in the EHR for were examined. Interventions included: BP control as a Performance Measure (PM), automatic notification to health care providers, reminder prompt in the EHR, and a systematic revisit schedule. In this cohort mean age was 68.6 ± 11.8 years and 94.5% were male. For patients declaring their race, 53.3% were white, 24.0% African American, and 21.1% were Hispanic. At baseline 44.6% of hypertensive patients were controlled and at the end of 2007, 73.1% were controlled. Percent controlled rates increased by 3.7% per year ($P < 0.0001$; 95% CI 3.5–4.0) during this period. At the end of the follow up period (August 2010) control rates were 79%. Yearly improvement in control rates by ethnicity were as follows for African American, Hispanic and Caucasian patients: For the period 2000–2006: 3.60%, 5.70%, 3.90%, for the period 2006–2010: 1.70%, 1.90% and 1.60% respectively ($P < 0.001$ comparing the two periods).

Conclusions: High rates of BP control were achieved across the board in all ethnic groups. Improvement in control rates continued until 2010, but yearly improvement was greater in 2000–2006 as compared to 2006–2010. Similar improvement was noted in all ethnic groups.

Keywords: Hypertension; Control; Ethnicity

FP-4

CLINICAL CHARACTERISTICS OF PATIENTS WITH UNCONTROLLED AND APPARENT TREATMENT RESISTANT HYPERTENSION: NHANES 1988–2008

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Background: While hypertension control to <140/<90 mmHg improved to 50% (NHANES 2007–2008), millions of patients remain uncontrolled. Defining characteristics of uncontrolled hypertensive patients may facilitate efforts to improve blood pressure (BP) control.

Methods: Subjects included 13 375 hypertensive adults from National Health and Nutrition Examination Surveys (NHANES) 1988–2008 subdivided into 1988–1994, 1999–2004, 2005–2008. Uncontrolled hypertension was defined as BP <140/<90 mmHg and apparent treatment resistant (aTRH) if the patient reported taking ≥3 antihypertensive medications. Framingham 10-year coronary risk (FCR) was calculated. Multivariate regression was used to identify independent predictors of untreated, treated uncontrolled, and aTRH.

Results: The majority of uncontrolled hypertensives were untreated across surveys. Multivariate predictors of untreated hypertension in all three NHANES survey periods, i.e., consistent, included male sex (odds ratio 2.26–2.73 95% confidence intervals [1.86–3.51]), infrequent (0–1) healthcare visits/year (4.66–4.95 [3.11–6.94]), body mass index <25 kg/m2 and <Stage 3 chronic kidney disease ([CKD], 1.67–2.28 [1.10–3.66] and FCR <10% (7.65–8.61 [4.78–12.26]). Most treated, uncontrolled patients reported taking 1–2 BP medications. Predictors of treated, uncontrolled hypertension across surveys included increasing age (1.19–1.30 [1.06–1.42]/10 years), black race/ethnicity (1.43–1.47 [1.13–1.85]), and FCR >20% (1.81–2.93 [1.27–3.86]). The percentage of uncontrolled hypertensives with aTRH increased over time (15.9% vs 28.0%, $P < 0.01$). Predictors of aTRH included obesity (2.04 [1.17–3.53], CKD (2.52 [1.75–3.62]) and FCR >20% (4.29 [1.95–9.42]) with age and black race/ethnicity significant in 2005–2008.

Conclusions: Strategies to increase healthcare use by people that are disproportionately male, lean and low 10-year FCR could improve hypertension treatment and control. Targeted strategies are needed to offset projected increases in uncontrolled treated and aTRH given population health trends to older age, more ethnic minorities, and a higher prevalence of obesity complicated by CKD and other coronary risk equivalents.

Keywords: Clinical characteristics; Uncontrolled; Treatment resistant; Hypertension

Featured Posters – Adolescent Hypertension

FP-5

WHICH BP MEASUREMENT METHOD BEST PREDICTS TARGET ORGAN DAMAGE IN YOUTH?

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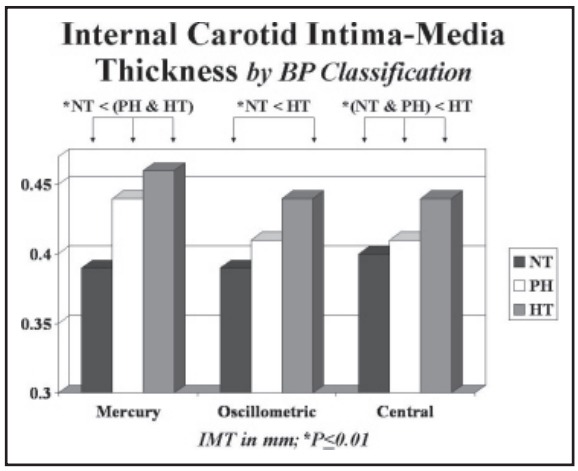
Hypertension (HT) is an important risk factor for target organ damage (TOD) in children and adults. However, new methods for measuring BP are replacing the gold-standard of mercury sphygmomanometry (BPm) in many clinics. Therefore, we sought to determine the utility of different BP measurement techniques in predicting sub-clinical TOD in adolescents and young adults. Subjects participating in a study of the CV effects of obesity and type 2 diabetes (DM) were evaluated (N = 775, 18 ± 3.3 years, 35% male, 59% non-Caucasian, 31% DM). We measured adiposity, lab, LVM, carotid IMT (cIMT) & arterial stiffness (augmentation index, AIx & pulse wave velocity, PWV; brachial artery distensibility, BrachD). BP was measured three times with mercury sphygmomanometery, an oscillometric device (BPo, DynaPulse, PulseMetric, San Diego, CA) and central aortic BP (BPc) was derived with arterial tonometry (SphygmoCor, Atcor Medical, Sydney, Australia). Subjects were stratified as normotensive (NT), pre-hypertensive (PH) or hypertensive (HT) based on BPm using 4th Report if < 18 and JNC7 if ≥18 years. For BPo and BPc, the 90th and 95th %ile for our lean subjects was used. Chi square



analyses was done to examine differences in prevalence of HTN by BP technique. Anova was used to determine differences in CV risk factors and TOD by BP group for the three BP techniques. The prevalence of HTN was high in this cohort with mean BMI of 31.6: BPo highest (36.7%), followed by BPc (18.8%) and BPm (9%), $P \leq 0.001$ for difference by BP technique. However, BPm was most consistent in identifying TOD. For all measures, stratification by BPm showed significant differences between NT and both PH and HT (all $P \leq 0.03$) while BPo and BPc were not able to detect differences between NT and PT for internal carotid IMT and AIx. We conclude that mercury sphygmomanometry should remain the gold standard for evaluation of HT and the risk for TOD in adolescents and young adults (figure 1).

Keywords: Hypertension; Adolescent; Target organ damage; BP measurement technique

FP-6

EFFECTS OF THE DASH DIET ON FLOW MEDIATED DILATION (FMD) IN ADOLESCENTS WITH PRE-HYPERTENSION AND HYPERTENSION

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Endothelial function, as measured by FMD, was compared among adolescents with elevated blood pressure (BP) who participated in either a 6-month clinic-initiated behavioral nutrition intervention emphasizing the DASH (Dietary Approaches to Stop Hypertension) diet or who received usual hospital-based nutrition care for BP management. Sixty-four adolescents with pre-hypertension or stage one hypertension, newly enrolled in a hospital-based hypertension clinic, were randomized to the DASH intervention (DASH, n = 33) or usual nutrition care (UC, n = 31). Exclusion criteria included being on BP altering medications, receiving prior formalized diet therapy to manage BP, presence of target organ damage, having diagnosed diabetes or an eating disorder. The DASH intervention included two counseling sessions with a dietitian on the DASH diet, six mailings, and 8 weekly and then seven bi-weekly telephone calls on behavioral strategies to promote dietary change. UC included two sessions with a dietitian on dietary guidelines consistent with those from the Fourth Pediatric Report of the National High Blood Pressure Education Program. Adolescents in both groups were prescribed calorie levels for weight maintenance. Weight, height and FMD were assessed at pre-treatment (baseline) and after the 6 month intervention. FMD was adjusted for pre-treatment arterial diameter at rest. Among completers (DASH, n = 27; UC, n = 24), post-treatment mean values for FMD were significantly greater among DASH participants relative to UC after adjustment for age, gender, race, BMI z score and pre-treatment FMD level (adjusted means + SD; 8.16% + 1.13 vs 5.29% + 0.76, $P = 0.04$). These findings suggest that a clinic-initiated behavioral nutrition intervention emphasizing the DASH diet with telephone and mail follow-up can lead to improved endothelial function in adolescents with above normal blood pressure over usual hospital-based nutrition care.
Supported by NIH Grant HL088567-01.

Keywords: Diet therapy; Endothelial function; Hypertension; Adolescents

FP-7

DETERMINANTS OF ARTERIAL STIFFNESS IN CHILDREN AND ADOLESCENTS

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Arterial stiffness as determined by carotid-femoral pulse wave velocity (PWV) has been shown to predict cardiovascular morbidity and mortality in adults. This cross sectional study aimed to examine the association of PWV with cardiovascular risk factors and inflammatory indices in young individuals. Eighty-four children and adolescents (mean age 13.1 ± 3 years, 56 boys) referred for elevated blood pressure were subjected to 24 hour ambulatory blood pressure (ABP) monitoring, anthropometric evaluation and PWV assessment and measurements of serum glucose, lipids, uric acid, homocysteine, adiponectin, leptin and high-sensitivity CRP (hs-CRP). Average systolic/diastolic ABP was 119.3 ± 12.1/66.7 ± 6.2 mmHg (16 subjects with ABP ≥ 95th centile), body mass index (BMI) 22.4 ± 4.7 kg/m2 (38 overweight/obese subjects) and PWV 6.5 ± 1.7 m/s. PWV was significantly correlated with age ($r = 0.39$), BMI (0.50), systolic ABP (0.36), uric acid (0.38), log triglycerides (0.33), HDL-cholesterol (−0.30), adiponectin (−0.27), log hs-CRP (0.26) and log homocysteine (0.32) (all $P < 0.05$). In stepwise multiple regression analysis only BMI was a significant independent predictor of PWV (beta ± SE 0.18 ± 0.04). From the lower to the higher BMI quartile, PWV, systolic ABP, uric acid, triglycerides, hs-CRP and leptin increased, whereas HDL-cholesterol and adiponectin dereased (all, $P < 0.05$). In conclusion, these data showed that in young individuals referred for elevated blood pressure, arterial stiffness assessed by PWV is associated with cardiovascular risk factors and inflammatory markers. However, BMI appears to be the main determinant of an adverse metabolic profile and increased PWV, suggesting a link between obesity and arterial stiffening from the young age.

Keywords: Arterial stiffness; Children; Blood pressure; Obesity

FP-8

PREVALENCE OF OVERWEIGHT AND ELEVATED BLOOD PRESSURE IN A LARGE COHORT OF CHILDREN AND ADOLESCENTS (AGE 3–17 YEARS) AT AN INITIAL CLINIC EXAMINATION

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The increasing numbers of children and adolescents with elevated blood pressure (BP) and overweight continue to be important public health problems. Data for this study were taken from a longitudinal pediatric cohort study based on electronic medical record (EMR) data of children (3–11 year) and adolescents (12–17 year) (total n = 244 523) from three large US health plans over the calendar period 1/1/07 to 12/31/09. Age-eligible subjects entered the cohort at the time of the first clinic visit in which blood pressure (BP) height, and weight were measured. Body mass index (BMI) percentiles were calculated using height, weight, gender, and age, based on the CDC-established reference growth charts, and BP percentiles were gender, age- and

height-specific, based on NHBPEP (Working Group) normative values. We report here BMI percentile and BP percentile measures collected at the first eligible clinic visit, based on single measures.
At entry, 58.3% of subjects were 3–11 years of age, 41.7% were 12–17 years, 50.1% were female. The percentage of children and adolescents with BMI $\geq$ the 85th percentile and BP $\geq$90th percentile in five age groups are presented in the Table.
As noted in the table, levels of overweight were high in all age categories, beginning at age 3, with similar percentages through age 17. These data suggest that efforts to prevent overweight and obesity need to target children at a very young age. Given the cross-sectional stability of the data, we speculate that excess weight and elevated BP have early onset and persist over time. Further analyses will evaluate tracking of BMI and BP percentile over time, and elucidate the impact of BMI on BP status.

Pediatric Hypertension Cohort, US, 2007–2009: Baseline BMI percentile and BP percentile according to age

n = 244,523	Baseline age (years)				
	3–5	6–11	12–14	15–17	All
Baseline BMI$\geq$ 85th percentile (%)	22.6	31.7	33.2	31.1	29.8
Baseline BP$\geq$ 90th percentile (%)	14.0	11.3	12.3	11.5	12.2

Keywords: Pediatric; Hypertension; Body mass; Longitudinal

Featured Posters – Cardiac Structure and Function

FP-9

PARALLEL DETERIORATION OF ALBUMINURIA, ARTERIAL STIFFNESS AND LEFT VENTRICULAR MASS IN ESSENTIAL HYPERTENSION: INTEGRATING TARGET ORGAN DAMAGE

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Left ventricular hypertrophy (LVH), albuminuria and arterial stiffening constitute established target organ damage. The aim of the study was to estimate whether increased urinary albumin excretion, assessed by albumin to creatine ratio (ACR), and carotid to femoral pulse wave velocity (c-f PWV) were accompanied by augmented LV mass index (LVMI) in hypertension.
In 428 non-diabetic untreated hypertensive subjects [257 men, mean age = 52 years, office blood pressure (BP) = 146/93 mm Hg] the distributions of ACR and c-f PWV were split by the median (8 mg/g and 7.8 m/s respectively) and accordingly subjects were stratified into those with high and low values.
Multiple regression analysis revealed that age, male sex, 24-hour systolic BP, ACR and c-f PWV were the independent predictors of LVMI (R^2 = 0.478, $P < 0.0001$). Among patients with low ACR (n = 198), those with high c-f PWV (n = 84) compared to those with low c-f PWV (n = 114) were characterized by increased LVMI (by 8.9 g/m^2, P = 0.012) and prevalence of LVH (30 vs 14%, P = 0.015). Similarly among patients with high ACR (n = 230), those with high c-f PWV (n = 123) compared to those with low c-f PWV (n = 107) exhibited heightened LVMI (by 13.6 g/m^2, P = 0.001) and prevalence of LVH (44 vs 25%, $P < 0.001$).
In conclusion, increased ACR in conjunction with pronounced arterial stiffness is accompanied by augmented LV mass and higher LVH rates, independently of established confounders in essential hypertensive subjects. Furthermore, the observed interrelationships between LVMI, albuminuria and c-f PWV, suggest parallel target organ damage progression.

Keywords: Microalbuminuria; Left ventricular hypertrophy; Pulse wave velocity

FP-10

THE PROGNOSTIC VALUE OF LEFT VENTRICULAR HYPERTROPHY IN THE VERY ELDERLY: THE PROTEGER STUDY

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Our aim was to investigate the prognostic value of left ventricular hypertrophy (LVH) and other cardiovascular (CV) structural and functional parameters in an oldest-old population. Data were limited with regards to the predictive significance of CV structural and functional abnormalities.
In 331 hospitalized elderly patients (mean age $\pm$ standard deviation: 87 $\pm$ 7 years), we studied CV structural and functional parameters, including intima-media thickness, pulse pressure, pulse wave velocity, LVH, E/A ratio and left ventricular ejection fraction (LVEF), assessed by blood pressure monitoring, tonometry, and ultrasonography. Then we investigated their associations with cardiovascular and all-cause mortality after a mean follow-up of 378 days. A total of 110 deaths occurred.
In quantitative analysis, left ventricular mass index (LVMI) was significantly higher in CV mortality group (P = 0.03) than in survivors, and LVEF was significantly lower in both CV and all-cause mortality groups (P = 0.03 and P = 0.002, respectively) than in survivors. In qualitative analysis, both concentric LVH and reduced LVEF were significantly associated with CV mortality, while only reduced LVEF was significantly related to all-cause mortality (P = 0.01). On the contrary, none of the arterial structural and functional abnormalities showed significant associations with mortality. After full adjustments, LVEF remained as the only predictor of CV and all-cause mortality (HR of 0.70 and 0.77, respectively).
In conclusion LVEF, among all measured cardiovascular parameters, was the only significant predictor of both CV and all-cause mortality in the elderly, independently of traditional CV risk factors.

Keywords: Left ventricular hypertrophy; Elderly population; Left ventricular geometry; Cardiovascular risk assessment

FP-11

CORNELL PRODUCT LEFT VENTRICULAR HYPERTROPHY IN ELECTROCARDIOGRAM AND MORTALITY IN A GENERAL POPULATION

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Background: Left ventricular hypertrophy (LVH), assessed by electrocardiogram, is associated with an increased risk for cardiovascular (CV) events among hypertensives. We evaluated

the risks of LVH for mortality in a Japanese general population without a history of CV or stroke events.

Method: We measured electrocardiogram and blood pressure in 10172 subjects at baseline. The Cornell product (CP) and Sokolow-Lyon (SL) voltage were calculated as markers of LVH (CP $\geq$ 2440 mm*msec and SL voltage $\geq$ 38 mm). Follow-up was performed for the average 10.8 $\pm$ 2.3 years, and the mortalities from any cause and combined CV and stroke causes were evaluated.

Results: The prevalence of CP-LVH and SL-LVH were 6.2% and 9.3%, respectively. There were 705 cases of death from any causes including 130 cases from CV or stroke events. CP-LVH was a significant predictor of mortality [any causes: hazard risk (HR) 1.81, 95% confidence interval (CI) 1.42–2.31, combined CV and stroke: HR 1.90, 95%CI 1.13–3.21] even after adjustment for confounding factors, but SL-LVH was a marginally significant predictor of mortality from any causes (HR 1.22, P = 0.066). In the parallel analysis in hypertensive subgroups, the risks of CP-LVH for total mortality were significant both in non-hypertensive (HR 1.86, P = 0.003) and hypertensive subjects (HR 1.78, $P < 0.001$); however, the risk of SL-LVH was significant only in hypertensive subjects (HR 1.33, P = 0.037).

Conclusion: Both CP-LVH and SL-LVH are risk factors for mortality from any causes in the Japanese general population. The predictive value of CP-LVH for total death is stronger than SL-LVH, and demonstrated in both non-hypertensive and non-hypertensive subjects.

Keywords: Electrocardiogram; Cornell product; Hypertension; Left ventricular hypertrophy

FP-12

IDENTIFICATION OF MYOCARDIAL VIABILITY IN HYPERTENSIVE PATIENTS RECEIVING BETA-BLOCKERS BY DOBUTAMINE ECHOCARDIOGRAPHY

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Background: The contractile response to dobutamine stimulation is attenuated in hypertensive patients receiving β-blockers. We attempted to demonstrate that increasing the infusion dose of dobutamine can improve the sensitivity of low dose dobutamine echo (DE) for the identification of myocardial viability in such patients.

Methods and results: Thirty hypertensive patients with chronic coronary disease and LV dysfunction elected for revascularization were studied with low dose DE (5 to 10 μg/kg/min) as well as with additional dobutamine infusions (up to 40 μg/kg/min). All pts had been taking β-blockers for at least 2 weeks before the test. Functional recovery was determined by a rest echo 3 months after revascularization. Of a total of 480 LV segments, 165 were classified as hypo- and 132 as akinetic on baseline echocardiography: 273 were successfully revascularized. Revascularization resulted in functional recovery in 75 of 143 hypokinetic (52%) and in 43 of 130 akinetic segments (33%, $P < 0.05$). The contractile reserve induced by low dose dobutamine infusion was markedly blunted by β-blockers. However, until 40 μg/kg/min, the sensitivity for predicting functional recovery was significantly dependent on the dobutamine dose increasing and the specificity was still acceptable during high dose dobutamine infusion.

Conclusions: In hypertensive patients treated with β-blockers, increasing dobutamine dose up to 30 μg/kg/min is advisable for the detection of myocardial viability. This approach avoids the withdrawal of β-blockers before the test and optimizes DE results.

Dobutamine dose (μg/kg/min)	10	20	30	40
Sensitivity (%) for all segments	31*	57†	72	75
Sensitivity for hypokinetic segments	43*	64	74	77
Sensitivity for ackinetic segments	12*	35‡	60	70
Specificity (%)	93	91	87	81

*$P < 0.01$, vs 20, 30, and 40; †$P < 0.05$ vs 30 and 40; ‡$P < 0.01$ vs 30, and 40 μg/kg/min.

Keywords: Hypertension; Myocardial viability; Beta-blocker; Dobutamine echocardiography

FP-13

TARGETED DELIVERY OF ENDOTHELIAL CELLS (ECs) OVEREXPRESSING IL8RA AND IL8RB RECEPTORS PROMOTES STRUCTURAL AND FUNCTIONAL RECOVERY OF THE LEFT VENTRICLE (LV) IN RATS FOLLOWING MYOCARDIAL INFARCTION (MI)

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Introduction: Interleukin receptors IL8RA and IL8RB on neurophil membranes bind to IL8 with high affinity and play a critical role in neutrophil recruitment (e.g. adhesion and trans-endothelial migration) to sites of infection and/or inflammation. The current study tested the novel hypothesis that administration of ECs overexpressing IL8RA and IL8RB can accelerate the adhesion of ECs to the injured tissue and effectively inhibit acute MI-induced LV remodeling and dysfunction.

Methods: Myocardial infarction (MI) was created by ligating the first and second diagonal branches of the left anterior descending coronary artery (LAD) in 12 week old male Sprague-Dawley rats. Rats with MI were divided into three subgroups: Group 1 received i.v. vehicle; Group 2 received i.v. ECs transfected with pAd-Null (empty adenoviral vector, total 1.5×10^6 cells at 1, 3, and 5 hour post MI); and Group 4 received ECs transfected with both pAd-IL8RA and pAd-IL8RB. Two wks post MI, echocardiographic analysis was performed to assess cardiac function. Rats were then euthanized and the LVs were cut into 2 mm slices perpendicular to the apex-base axis. Five micrometer cross sections of each cardiac slice were stained with picosirus red for collagen volume measurement as an index of infarct size.

Results: Comparisons of infarct size for rats received ECs that overexpress IL8RA and/or IL8RB are shown in the figure (results are means $\pm$ SEM, *$P < 0.05$ vs control). IL8RA/RB-EC treatment decreased infarct size and improve the MI-induced LV dysfunction, as seen by an increase in LV ejection fraction.

Conclusion: These provocative findings suggest that ECs overexpressing IL8RA and IL8RB mimic the behavior of neutrophils that target and adhere to injured tissues, thus minimizing the inflammatory response to injury. Targeted delivery of ECs to infarcted hearts provides a novel strategy for the treatment of acute MI in humans.

Keywords: Myocardial infarction; Endothelial cells; IL8RA/IL8RB receptor; Left ventricle

Poster Session I
Adolescent Hypertension and Obesity

PO-1

COMMON CAROTID ARTERY INTIMA-MEDIA THICKNESS IN PATIENTS WITH ABDOMINAL OBESITY AND ESSENTIAL HYPERTENSION

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Introduction: Abdominal obesity (AO) and arterial hypertension (AH) are atherosclerosis risk factors. Increased intima-media thickness (IMT) of the common carotid artery (CCA) is an early sign of atherosclerosis.

Material and methods: Two hundred and sixteen patients with AO and 23 healthy controls aged 30–55 years were examined. None of them had clinical manifestations of atherosclerosis. All of them underwent ultrasound duplex scan of common carotid arteries (ALOKA SSD – 3500, Japan). Increased IMT CCA above 0.9 mm was considered to be pathological. Atherosclerotic plaque was defined as local thickening of the arterial wall increasing by 50% or more normal adjacent intima-medial complex which differed from normal artery wall and/or increased IMT >1.3 mm.

Results: AH was revealed in 60.9% patients with AO. In obese patients with IMT [lte] 0.9 mm systolic blood pressure (BP) was lower than in patients with IMT >0.9 mm (132.2 ± 1.5 mm Hg and 138.6 ± 2.4 mm Hg accordingly, $P < 0{,}01$). IMT in hypertensive patients with AO was higher than in obese patients with normal BP (0.90 ± 0.02 mm vs 0.82 ± 0.02 mm accordingly, $P < 0.01$). IMT of CCA in normontensives with AO was higher than in non-obese controls (0.72 ± 0.03 mm vs 0.55 ± 0.02 mm, $P < 0.01$). Atherosclerotic plaques were found in 39.8% patients with AO. Furthermore, the rate of increase of IMT above 0.9 mm did not differ between normontensive patients with AO and obese hypertensives (49.4% and 69.8% accordingly, $P > 0.05$).

Conclusion: In patients with AO associated with hypertension IMT of CCA as well as the rate of increase of IMT are higher than in obese normotensives. In AO normal BP vascular remodeling was observed in 49.4% of patients.

Keywords: Abdominal obesity; Arterial hypertension; Intima-media thickness.

PO-2

PREVALENCE OF HYPERTENSION IN PEDIATRIC ONCOLOGY SURVIVORS

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Background: Retrospective studies suggest that pediatric oncology survivors are at risk for hypertension.

Objectives: To establish the prevalence of hypertension in long-term pediatric oncology survivors, using casual and 24-hour ambulatory blood pressure monitoring.

Methods: We prospectively studied two cohorts of pediatric patients diagnosed with cancer and treated with chemotherapy 5 and 10 years previously, who were seen at BC Children's Hospital Oncology Long-Term Follow-Up Clinic from June 2009-July 2010. Primary goal was to identify the four diagnoses of: normotension, masked HTN, white coat HTN, and true HTN. We analyzed for 95th percentile casual BP index, 24-hour ABPM 95th percentile index, BMI and height *Z*-scores, eGFR with Schwartz formula (<18 yo) or MDRD (≥18 yo), and microalbuminuria.

Results: Seventy-eight pts were eligible, 44 (61% males) were enrolled. Mean age at diagnosis was 5.0 ± 3.9 years. Most common diagnosis was ALL (n = 23, 52%). Mean age at follow-up was 14.1 ± 4.3 years. Only 9% (4/44) had 95th precentile casual SBP or DBP index > 1.0. 64% (28/44) completed 24-hour ABPM. 22% (4/18) had BP abnormalities in the 5 year cohort, and 10% (1/10) in the 10 year cohort. Obesity was uncommon and the BMI *Z*-score median was 0.35, inter-quartile range (−0.2 to 0.98). Height *Z*-score median was 0.29, inter-quartile range (−0.1 to 1.1). 46.5% (20/44) pts had positive family history of HTN. None had prior history of chronic HTN.
46.5% (20/43) had eGFR <90 mL/min/1.73 m^2; 56% (10/18) in 10 year cohort, and 40% (10/25) in 5 year cohort. Only 2.3% (1/43) had eGFR <75 mL/min/1.73 m^2. Only 5.4% (2/37) had microalbuminuria.

Conclusion: We observed a high prevalence of undiagnosed hypertension (17%) and CKD (46%) in this non-obese cohort of pediatric cancer survivors. Hypertension and CKD prevalence did not have temporal correlation with time of diagnosis in this small study. There was a strong family history of hypertension (46%). Masked hypertension was identified in 14%, suggesting that standard clinic measures are insufficient at detecting blood pressure abnormalities in this population. Future prospective studies for monitoring renal health of pediatric cancer survivors should include 24-hr ABPM, and estimated GFR.

Systolic or Diastolic Hypertension		
	ABPM < 95th	ABPM ≥ 95th
Casual BP < 95th	78.6%	14.3%
Casual BP ≥ 95th	3.6%	3.6%

Keywords: Hypertension; Oncology survivors; Pediatrics

PO-3

BLOOD PRESSURE VARIABILITY IN WHITE COAT HYPERTENSIVE ADOLESCENTS

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To determine the blood pressure (BP) variability (BPV) in white coat hypertensive (WCH) adolescents, it was conducted a prospective and transversal study that included 90 male subjects (mean-age: 15 ± 1.4 years), who were underwent 24-hour ambulatory BP monitoring (ABPM) to obtain ambulatory BP during 24-hour, awake and asleep periods. The systolic and diastolic BPV were expressed as the standard deviation of the obtained values in each studied period. The presence of WCH was defined as casual BP higher or equal to 95th percentile and awake BP less than 95th. The homogeneity variance test and the variance ratio test (*F*-test) were applied to compare the BPV among WCH, sustained hypertensives and normotensives. The WCH prevalence was 53.3% (n = 48). Adolescents with WCH showed significant higher values than normotensives in casual and ambulatory BP during all periods, these values were (systolic/diastolic, mmHg)): 138 ± 12/72 ± 7 vs 116 ± 8/63 ± 9 for casual BP, 123 ± 7/69 ± 5 vs

114 ± 6/64 ± 5 for 24-hour BP, 124 ± 7/71 ± 6 vs 116 ± 6/66 ± 5 for awake BP and 113 ± 10/59 ± 7 vs 103 ± 6/54 ± 4 for asleep BP ($P < 0.0001$). The F-test showed that systolic BPV during awake period in WCH was statistically significant higher than in sustained hypertensives [7.14 vs 3.56 ($P < 0.01$)], but did not show any significant differences with normotensives [7.14 vs 5.99 (P = NS)]. However, the highest values of systolic BPV during asleep period were showed by adolescents with WCH [9.55, 7.03 and 5.67 for WCH, sustained hypertensive and normotensive, respectively, ($P < 0.01$)]. In conclusion, there is a very high WCH prevalence in male adolescents. In this age group, only nocturnal systolic BPV is associated with the presence of WCH, showing this condition the highest levels of systolic BPV, even above the sustained hypertension. These conditions, WCH and higher nocturnal systolic BPV, are extremely important because from the early age the subjects could be in cardiovascular risk.

Keywords: White coat hypertension; Adolescentes

PO-4

WITHDRAWN AT AUTHORS' REQUEST

WITHDRAWN AT AUTHORS' REQUEST

PO-5

PHARMACOLOGIC MANAGEMENT OF PRIMARY HYPERTENSION IN ADOLESCENTS

Esther Yoon, Lisa Cohn, Albert Rocchini, David Kershaw, Gary Freed, Frank Ascione, Sarah Clark. University of Michigan.

Background: Prevalence of primary hypertension (HTN) in adolescents is increasing but pharmacologic management of primary HTN in adolescents has not been well-described.

Objective: To describe antihypertensive (antiHTN) prescribing patterns for adolescents with primary HTN.

Design/Methods: Longitudinal analysis of 2003–2008 Michigan Medicaid claims data for adolescents 12–18 years who had 3 + years of Medicaid enrollment (11 ± months per year). We identified adolescents with primary HTN by ICD-9 codes and looked at prescription (Rx) patterns chronologically for antiHTN drug class prescribed (if any) and the specialty of prescribing physician. We also examined patient demographics and presence of obesity-related comorbidities (obesity, dyslipidemia, metabolic syndrome, diabetes type2).

Results: During 2003–2008, there were 4974 adolescents with primary HTN; 22% (1070) received antiHTN Rx. Overall, 66% were boys; 63% were 12–14 years old; 54% Black, 41% White and 4% Hispanic; 48% had obesity-related comorbidity. Whites (OR 1.61; CI 1.39–1.86); older adolescents ≥15 years (OR 1.77; CI 1.54–2.04) and those with obesity comorbidity (OR 1.67; CI 1.45–1.92) were more likely to receive antiHTN Rx controlling for gender, age, race and comorbidity in logistic regression. More than 1/4 of adolescents who received antiHTN Rx got combination therapy; ACE inhibitors were the most frequently prescribed, both for monotherapy and combination therapy (Table). More than 2/3 of adolescents received antiHTN Rx from primary care physicians (pcp) only, and these pcps prescribed most combination therapy.

Conclusions: Race differences exist in physicians' prescribing of antiHTN Rx to adolescents with primary HTN. Adult pcps were leading prescribers of antiHTN Rx for adolescents with primary HTN. The substantial number of adolescents with combination antiHTN Rx suggests difficulty reaching blood pressure goals on monotherapy. The underlying rationale in decision to treat adolecsents with primary HTN by physicians of different specialties warrants further study.

Medicaid adolescents with primary HTN and antiHTN Rx, by drugclass and prescribing physician

	ACE	ARB	BB	CCB	DIU	Combo	Total
Pcp only (Adult pcp only)	199 (172)	4(2)	135 (129)	58(48)	145 (122)	196 (177)	737(69%)
Spec only	29		33	8	27	21	118(11%)
Pcp+Spec	36	2	22	14	17	62	153(14%)
Unknown	12		13	8	19	10	62(6%)
Total	276 (26%)	6 (1%)	203 (19%)	88 (8%)	208 (19%)	289 (27%)	1070

Keywords: Primary hypertension; Adolescents; Variation in care; Primary care

Antiatherosclerotic Drugs

PO-6

EFFECTS OF 3-HYDROXY-3-METHYLGLUTARYL COENZYME A REDUCTASE INHIBITORS ON BLOOD PRESSURE

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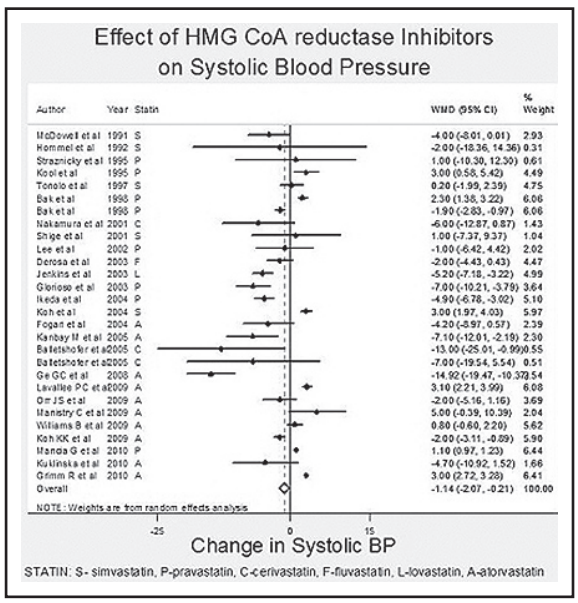
Background: In experimental studies, statins have been shown to have a beneficial effect in lowering blood pressure through increased NO bioavailability by the endothelium, decreased reactive oxygen species production and improved arterial compliance. Statins reduce the risk of cardiovascular events in people with hypertension. This benefit could arise from a beneficial effect of statins on blood pressure control.

Methods: We performed a meta-analysis of the effect of statins on systolic blood pressure (SBP) and diastolic blood pressure (DBP) including prospective randomized, controlled trials of statin therapy in which concomitant antihypertensive treatment (if any) remained unchanged throughout the study. A MEDLINE search was conducted (1991–2010) for studies in which patients were randomized to treatment with a statin plus standard treatment (or placebo) vs standard treatment (or placebo), and data on SBP and DBP, before the treatment initiation and at the end of the follow-up period. A random effect analysis was conducted based on the Der-Simonian and Laird model. Small study bias was examined with funnel plot analysis.

Results: A total of 26 studies with 28 comparison groups, examining 1208 controls, 1339 patients on statins and 243 crossover patients were examined. Overall, the patients on statins showed a small but statistically significant change in both SBP and DBP. The mean SBP in the statin group was lower by 1.14 mm Hg (95% CI: 0.21 to 2.07). Also, the mean DBP in the statin group was lower by 0.8 mm Hg (95% CI: 0.3 to 1.3).

Conclusion: In our meta-analysis of prospective controlled studies looking at 2790 patients, there is a small but significant reduction of SBP and DBP in patients taking statins. Hence, the benefits of statins in reducing cardiovascular events are a direct consequence of their lipid-lowering and pleiotropic effects, part of which is mediated by their blood pressure lowering action.

Keywords: HMG CoA reductase inhibitors; Blood pressure



PO-7

STATIN EFFECT ON THE BLOOD PRESSURE IN YOUNG AND ELDERLY ADULTS: META-ANALYSIS

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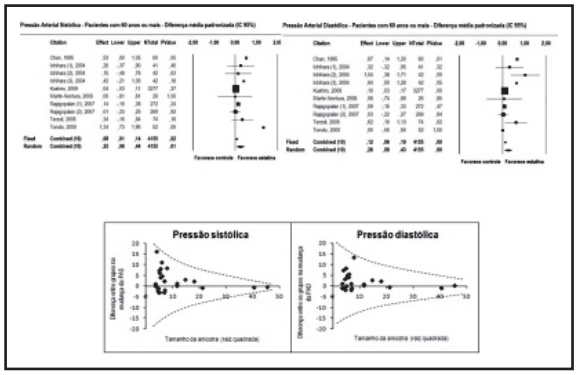
The elderly population shows high prevalence of hypertension, which is mostly related to hypercholesterolemia and diabetes. Therefore, the statins are frequently prescribed in this age group, with the objective of lowering the LDL cholesterol levels, although other effects have been studied. The objective of this study is to analyze whether or not there is impact on the use of statins on the blood pressure in elderly population. A meta-analysis was done with 19 randomized, controlled, double-blind trials, with a total of 10 955 patients, 37.9% of these elderly. The effect of therapy with statins on systolic blood pressure (SBP) in the total sample was a reduction with a padronized mean difference (PMD) of 0.36 ($P < 0.001$). However, the trials with the elderly population show a reduction of the SBP of only 0.25 ($P = 0.01$), while the SBP reduction in the trials involving mean age lower than 60 years old was of 0.48 ($P < 0.001$). There was also a reduction of the diastolic blood pressure (DBP) in the general population, with a PMD of 0.48 ($P < 0.001$), while in the elderly population alone the reduction was of 0.26 in PMD ($P < 0.001$), and in the non elderly adult population of 0.67 in PMD ($P < 0.001$). In conclusion, the statins cause a reduction of the arterial pressure of the elderly, although it is less significative than the reduction in the population of age less than 60 years old.



Keywords: Hypertension; Statin; Elderly.

Cardiac Structure and Function/Imaging

PO-8

EFFECT OF TELMISARTAN ON PAROXYMAL ATRIAL FIBRILLATION IN HYPERTENSIVE PATIENTS WITH DIFFERENT LEFT ATRIAL SIZE

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Aim of this study was to evaluate the effect of telmisartan (T) and amlodipine (A) on atrial fibrillation (AF) recurrence in hypertensive patients with paroxymal AF and normal or increased left atrial (LA) size.

We studied 288 mild hypertensive outpatients in sinus rhythm but will at least 2 ECG-documented episodes of AF in the previous 6 months; half of them had an inferior-superior LA dimension <45 mm, and the other half >45 mm. The patients were randomized to T 80–160 mg/od (n = 72 with LA <45 mm, n = 72 with LA >45 mm) or to A 5–10 mg/od (n = 72 with LA <45 mm, n = 72 with LA >45 mm) for 1 year. Blood pressure and a 24 hour ECG were evaluated monthly. Patients were asked to report any episode of symptomatic AF and to perform an ECG as early as possible.

SBP and DBP were significantly and similarly reduced by the two treatment ($P < 0.001$ vs baseline) in the four groups of patients. Among those with LA dimension >45 mm a total of 35 (48.6%) patients treated with A had a recurrence of AF as did 18 (25%) patients treated with T ($P < 0.05$ vs A) Among the patients with LA dimension <45 mm a total of 23 (31.9%) patients treated with A had a recurrence of AF as did 8 (11.1%) patients treated with T ($P < 0.01$ vs A).

Despite a similar BP lowering T was more effective than A in preventing new episodes of AF and it was particularly evident in patients with normal LA size. It suggest that in this type of patients ARB treatment is to prefer to Ca blocker treatment and that earlier it is begun greater is the prevention of AF recurrences.

Keywords: Telmisartan; Amlodipine; Atrial fibrillation; Atrial enlargement

PO-9

EFFECT OF ALISKIREN ON QT DISPERSION IN DIABETIC AND NON DIABETIC HYPERTENSIVE PATIENTS

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Aim of this study was to compare the effect of aliskiren on QT dispersion in hypertensive patients with or without diabetes.

After a 2 week placebo period 98 mild hypertensive patients with well controlled type 2 diabetes (HbA_1c <7%) and 102 mild hypertensive patients without diabetes were treated with aliskiren 300 mg for 12 weeks. At the end of the placebo period and of treatment period BP was evaluated and an ECG was recorded using a paper speed of 50 mm/s. The QT intervals were measured manually in all the 12 leads in blinded fashion and three consecutive QT intervals were measured and averaged for each lead. The QT dispersion was corrected for the heart rate (QTc).

The treatment induced a significant and similar SBP/DBP reduction in both groups of patients ($P < 0.001$ vs baseline). In hypertensive patients with type 2 diabetes aliskiren induced a significant reduction in QTc dispersion (-10.6 ± 22.6 ms, $P = 0.03$) and in QTmax (-12.1 ± 22.1 ms, $P = 0.02$); the QTc dispersion change did not correlate with BP change. In hypertensive patients without diabetes aliskiren induced a smaller and non significant reduction in QTc dispersion (-4.8 ± 19.6 ms, $P = 0.09$) and in QTmax (-3.9 ± 19.6 ms, $P = 0.11$).

Aliskiren reduces QT dispersion in hypertensive diabetic patients and this effect is not related to the BP lowering. It suggests that aliskiren has the potential to reduce severe arrhytmic complications in this type of patients.

Keywords: Aliskiren; QT dispersion; Diabetes; Hypertension

PO-10

IMPACT OF ANTIHYPERTENSIVE THERAPY ON DYSSYNCHRONY IN PATIENTS WITH NEVER-TREATED HYPERTENSION

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Background: The impact of antihypertensive therapy on dyssynchrony in patients with never-treated hypertension has not been explored.

Methods: Sixty patients of never-treated hypertension (53.3% men, mean age 54.3 ± 9.7 years) underwent dyssynchrony evaluations at baseline and after 6 months of antihypertensive therapy as follows: (1) standard deviation (SD) of time from ECG Q to systolic peak velocity of 12 Left ventricular (LV) segments (ms, Ts-SD12) and maximum difference of time to systolic peak velocity among 12 LV segments (ms, Ts-Max) (systolic dyssynchrony); (2) SD of time from ECG Q to early diastolic peak velocity of 12 LV segments (ms, Te-SD12) and maximum difference of time to early diastolic velocity among 12 LV segments (ms, Te-Max) (diastolic dyssynchrony); (3) Inter-ventricular mechanical delay (IVMD) was defined as the difference of LV and RV pre-ejection periods (interventricular dyssynchrony); (4) sum of time exceeding aortic closure in strain curves of 12 LV segments (ms, oExcT) (contractile diastolic dyssynchrony). Ts-SD12 ≥ 33 ms or Ts-Max ≥100 ms was regarded as systolic dyssynchrony. Patients without systolic dyssynchrony (group 1, N = 31) and with systolic dyssynchrony (group 2, N = 29) at baseline were compared.

Results: In group 2, LV systolic (Ts-SD12, Ts-Max) and diastolic (Te-Max) dyssynchrony significantly improved after antihypertensive therapy. However, there were no significant differences except oExcT in group 1.

Conclusion: Antihypertensive therapy could reverse the dyssynchrony parameters of echocardiography in patients with never-treated hypertension and, in particular, systolic dyssynchrony.

Effects of antihypertensive therapy on dyssynchrony

Mean Change (95% CI)	HT without systolic dyssynchrony (n = 31)	HT with systolic dyssynchrony (n = 29)
LV systolic dyssynchrony		
ΔTs-Max (ms)	4.7 (-16.8 to 26.1)	-34.0 (-55.2 to -12.9)*
ΔTs-(lateral-septal) (ms)	10.7 (-3.5 to 24.9)	-31.6 (-50.9 to -12.4)*
LV diastolic dyssynchrony		
ΔTe-SD12 (ms)	−0.7 (−5.6 to 4.3)	−3.0 (−7.4 to 1.3)
ΔTe-Max (ms)	−1.6 (−16.1 to 13.0)	−14.2 (−28.2 to −0.2)*
Interventricular dyssynchrony		
ΔIVMD (ms)	-2.8 (-8.7 to 3.2)	2.4 (-3.4 to 8.3)
Contractile diastolic dyssynchrony		
ΔoExcT (ms)	-126.4 (-243.8 to -9.0)*	-128.7 (-275.4 to 18.0)

*$P < 0.05$ vs baseline.

Keywords: Hypertension; Dyssynchrony; Antihypertensive therapy; Echocardiography.

Comprehensive Multi-Level Interventions for Hypertension Management in High-Risk Groups

PO-11

REFRACTORY HYPERTENSION CHARACTERIZED BY HEIGHTENED SYMPATHETIC TONE

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Among patients with resistant hypertension (RHTN), there appears to be a subset of patients whose blood pressure (BP) remains uncontrolled in spite of maximum medical therapy. This prospective analysis aims to characterize this subset of patients whose BP is refractory to treatment (defined as uncontrolled BP after ≥6 months of follow-up in a hypertension clinic). Patients with controlled RHTN served as controls. 11 patients with refractory hypertension and 19 patients with controlled RHTN were included in the analysis. Age, race, gender, body mass index, plasma aldosterone, plasma renin activity, 24-hour urinary aldosterone excretion, brain natriuretic peptide, and C-reactive protein values were similar between the two groups. Patients with refractory hypertension had a significantly higher baseline heart rate. Twenty 4 hour urine metanephrine excretion and augmentation index also tended to be higher in patients with refractory hypertension compared to controls but the difference did not reach statistical significance. The following table summarizes our data:
The above data indicate that aldosterone excess is not the cause of refractoriness to treatment. The higher baseline heart rate, and a trend towards higher urinary metanephrines and higher augmentation indices in patients with refractory hypertension indicate that a heightened sympathetic drive or increased peripheral resistance contributes to the difficult to control BP in these patients.

Table I. Baseline characteristics of patients with refractory and controlled resistant hypertension

Parameter (Mean)	Refractory hypertension	Controlled RHTN	*P* Value
Age (years)	48 ± 14	58 ± 14	0.071
African American ethnicity (%)	64	45	0.337
Female gender (%)	73	55	0.329
Baseline SBP (mmHg)	169 ± 30	156 ± 21	0.22
Baseline HR (bpm)	81 ± 9	71 ± 11	0.033
BMI (kg/m^2)	33 ± 7	31 ± 7	0.252
Plasma aldosterone (ng/dL)	10 ± 8	13 ± 13	0.543
PRA (ng/mL/h)	2.8 ± 6.0	1.2 ± 1.3	0.254
24 hr urine aldosterone (ug/24 hour)	12 ± 12	14 ± 12	0.906
BNP (pg/mL)	59 ± 57	58 ± 71	0.244
hsCRP (mg/L)	10 ± 14	12 ± 24	0.840
24 hr total urine metanephrine (mg/24 hour)	604 ± 204	423 ± 205	0.064
Augmentation index (HR 75)	27 ± 10	18 ± 11	0.066

SBP, Systolic BP; DBP, Diastolic BP; HR, Heart rate; BMI, Body mass index; PRA, Plasma renin activity; BNP, Brain natriuretic peptide; hsCRP, high sensitivity C-reactive protein.

Keywords: Resistant hypertension; Refractory hypertension; Sympathetic tone; Peripheral vascular resistance

PO-12

PREHYPERTENSION HAS INCREASED PERIPHERAL RESISTANCE IN PATIENTS WITH OBESITY

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Introduction: During recent years we discuss whether borderline blood pressure levels require treatment. This new category is a continuum from prehypertension to hypertension and is a risk factor for cardiovascular disease. It is well accepted that in specific subgroups with specific concomitant diseases blood pressure in the prehypertension range should be treated.However we don't know about more hemodynamics data of these *P*.

Objective: The aim of this study was evaluate total peripheral resistance (TPR) and central blood pressure in patients (P) with prehypertension and obesity (PHTAO) compared with normotensive P (NORMP).

Material and methods: We studied 23 P with PHTAO (52 ± 3 years old), and 30 normotensive P diagnosed by ABPM in which we measured peripheral blood pressure (PBP), central blood pressure (CBP) and total peripheral resistance.

Results: Data from those *P* were compared and show in the following table:

Conclusions: Obese patients with prehypertension, have not been only significantly higher TPR than normotensive persons but also higher CBP indicating that they have more cardiovascular risk. This specific group, could be a target to start a proper treatment before appearing negative consequences.

Results of the two groups

DATA	SCBP	DCBP	CPP	TPR	S/D PBP
SAS	129 ± 3*	86 ± 4*	45 ± 3*	1.5 ± 0.2*	152/96 ± 9/6*
NORMAL	98 ± 2	78 ± 3	26 ± 4	1 ± 0.1	124/81 ± 3/4

*Means *P* value less than 0.05.

Keywords: Prehypertension; Obesity; Peripheral resistance; Risk factor

PO-13

SOME FIXED COMBINATIONS ARE BETTER REDUCING CENTRAL BLOOD PRESSURE AND HYPERTENSIVE TIME THAN OTHERS

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Introduction: Today we have several fixed combinations (FC) of drugs as an option to treat hypertensive patients (HTAP). However, it is important to know the differences between them to make the better choice.

Objective: We studied two different FC to know which of them can give us the better control of HTAP referring to reduce the central blood pressure (CBP) and augmentation index (AI).

Material and methods: We studied 40 HTAP, who received 20 mg enalapril+ 10 mg lercanidipine (GROUP, I) and 38 HTAP

treated with 5 mg felodipine+50 mg metoprolol (GROUP II). In all of them, we measured after 6 months of treatment: systolic and diastolic peripheral blood pressure (PSBP,PDBP), central systolic and diastolic blood pressure (CSBP,CDBP), hypertensive time during the day (DHT)in minutes, and AI.

Results: Data were compared and showed below:

Conclusions: Despite we have several options regarding fixed combinations to treat HTAP, not all of them have been equally efficacy. Lercanidipine+enalapril, show significantly better results to reduce HTAP vascular risk,taking into account that reduced much better CSBP, AI and also the DHT of these P compared with group II.

Results of the two fixed combinations						
Data	PSBP	PDBP	CSBP	CDBP	DHT	AI
Group I	134 ± 4	82 ± 3	105 ± 4*	79 ± 3	156 ± 11*	19 ± 3*
Group II	135 ± 4	83 ± 4	124 ± 6	81 ± 3	385 ± 14	29 ± 5

*Means P value <0.05.

Keywords: Fixed combinations; Lercanidipine; Enalaprilo

PO-14

PREVALENCE OF ORTHOSTATIC HYPOTENSION AMONG VERY ELDERLY PERSONS WITH HYPERTENSION

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While older Americans have a very high prevalence of hypertension, many of these patients also have orthostatic hypotension (OH). The prevalence of OH varies in different populations and increases with age. In the Cardiovascular Health Study, the prevalence of OH was 14.8% for persons aged 65–69 and 26% for those aged 85 and older. In elderly individuals, OH is a frequent cause of falls, which may result in serious complications, such as fractures and head injuries, syncope, brain hypoperfusion with cognitive decline, fear of falling, impaired quality of life, and increased risk of stroke and death.

The mechanisms responsible for orthostatic hypotension among the elderly are complex and may include volume depletion, autonomic dysfunction, arterial stiffness, cardiac diseases, central nervous system disorders, dementia, venous diseases, and amyloidosis. However, the use of antihypertensive medications is probably the most common cause.

In this study, we screened 94 very elderly residents in the Los Angeles Jewish Home for the Aging, who had a history of hypertension and were taking anti-hypertensive drugs. Among these participants, the average age was 89.8 ± 6.2 years and 70% were female. Forty-eight out of 94 (51%) participants manifested orthostatic hypotension. Patients with OH were more likely to have suffered from a stroke and TIA, hypothyroidism, or to be on anti-psychotic drugs.

In conclusion, OH is very prevalent among very elderly patients, particularly those with co-morbidities. The impact of OH on the morbidity and mortality of very elderly persons needs to be more closely scrutinized.

Keywords: Orthostatic hypotension; Elderly; Anti-hypertensive drugs

PO-15

EFFECTS OF RENAL STENTING ON RENAL AND CARDIAC OUTCOMES IN PATIENTS WITH RESISTANT HYPERTENSION

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The clinical evidence of the benefit of percutaneous revascularization of atherosclerotic renal artery stenosis is limited and recent studies have questioned the usefulness of renal artery stenting (NEJM 361: 1953, 2009). In a prospective observational study we have examined the effects of renal angioplasty with stenting in 36 hypertensive patients with resistant hypertension (age 68 ± 3 year; 25 M/11 F) and angiographically detected renal artery stenosis. Angiography was performed in patients in whom renal artery stenosis was screened either by angio-CT scan (n = 15), angio-MRI (n = 12), renal echo-Doppler (n = 2), renal scintigraphy (n = 2), or in patients with indication for peripheral arterial disease (n = 3). In all patients renal artery stenosis was greater than 80%. In these patients we assessed the effects of renal stenting on blood pressure, need for antihypertensive drugs, and renal and cardiac outcomes. At the time of revascularization we measured serum creatinine, 24-hour creatinine clearance (CrCl), 24-hour urinary protein excretion (UPE) and the urinary albumin/creatinine ratio (Ualb/Ucr). Patients were reassessed after 4 weeks, 6 months, and 4.5 years. Echocardiopraphy was performed at the time of revascularization and at the end of the follow-up. The number of antihypertensive drugs needed to control BP was significantly lower at the first (2.0 ± 1.5, $P = 0.022$) and second (2.1 ± 1.3, $P = 0.002$) follow-up visits, but it was comparable with baseline (2.6 ± 1.5) at the end of the follow-up (2.6 ± 1.3). BP decreased significantly across the whole study (baseline 160 ± 21/86 ± 13 mm Hg; first visit 144 ± 15/79 ± 10, $P = 0.005$; second visit 135 ± 10/75 ± 11, $P < 0.001$; third visit 140 ± 14/76 ± 9, $P < 0.001$). No significant changes in CrCl (baseline 62 ± 33 mL/min/1.72 m^2; first visit 70 ± 28; second visit 66 ± 31; third visit 65 ± 23), UPE, and Ualb/Ucr were detected between baseline and the follow-up visits. No significant changes were detected in left ventricular morphology (baseline LVMI 111 ± 37 g/m^2, third visit 101 ± 26) and systolic (baseline EF 67 ± 8%, third visit 66 ± 6) and diastolic function (baseline E/A ratio 0.83 ± 0.28, third visit 0.96 ± 0.34) after renal revascularization. In summary, revascularization of RAS provides stable improvement of BP and prevents worsening of renal function, whereas it does not affect cardiac structure and function.

Keywords: Renal artery stenosis; Resistant hypertension; Secondary hypertension; Atherosclerosis

PO-16

EVALUATION OF A TREATMENT ALGORITHM USING COMBINATION THERAPY FOR THE MANAGEMENT OF PATIENTS WITH HYPERTENSION AND HYPERCHOLESTEROLEMIA (STITCH2)

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Despite improving rates of hypertension control, management of patients with both hypertension and dyslipidemia remains problematic. Based on our evidence of improved control rates utilizing

a simplified algorithm in the management of hypertension, we proposed to determine if a simplified comprehensive treatment algorithm featuring initial use of single pill combinations (SPCs) would improve management of patients with both hypertension and dyslipidemia. To achieve this we studied 35 primary care practices in Ontario randomized to either guidelines-based care or to a simplified algorithm for management of patients with hypertension and dyslipidemia (STITCH2 care). Physicians randomized to the STITCH2 algorithm were trained to use an SPC combining an ACE inhibitor/angiotensin II blocker with diuretic, followed by an SPC combining a CCB with statin, followed by other adjunctive therapy as required. Physicians randomized to the guidelines-based care were instructed in current Canadian guidelines.

Practices enrolled $\leq$50 patients with a history of both risk factors and at least one risk factor above target. The impact of treatment was assessed at the cluster (practice) level. The primary endpoint was the control rate for both BP and LDL at 6 month follow-up. At baseline, mean ($\pm$ SD) BP was 144/85 $\pm$ 16/11 mm Hg and LDL was 117 $\pm$ 43 mg/dL. Elevated BP and LDL were present in 88% and 68% of patients, respectively. The primary endpoint – proportion of practice with BP and LDL at target after 6 months- was 31.3 $\pm$ 24% with STITCH2 care, vs 28.1 $\pm$ 15% with guidelines-care ($P > 0.1$). However, similar to findings in STITCH, STITCH2 care resulted in greater reduction in systolic BP (STITCH2-care: 16.2 $\pm$ 9 mm Hg, Guidelines-care: 10.1 $\pm$ 7 mm Hg, $P = 0.04$). LDL reduction was only marginally greater in STITCH2 practices (STITCH2: 17.4 $\pm$ 7.8 mg/dL, Guidelines: 13.6 $\pm$ 9.7 mg/dL, $P > 0.1$).

The STITCH2 care algorithm resulted in greater use of any SPC compared to guidelines care (73.8% vs 26.5%; $P < 0.01$) and greater use of the SPC of CCB/statin (31.2% vs 5.4%; $P < 0.01$).

These data confirm the value of simple algorithms emphasizing the use of SPCs for managing hypertension. However a single comprehensive algorithm targeting both hypertension and dyslipidemia did not perform better than guidelines-based care in the management of patients with multiple risk factors.

Keywords: Single pill combination; Hypertension; Dyslipidemia; Adherence

PO-17

SEX DIFFERENCES IMPACT THE HEMODYNAMICS OF UNTREATED ESSENTIAL HYPERTENSIVE SUBJECTS

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Knowledge of hemodynamic factors facilitates tailoring antihypertensive therapy and improves blood pressure control. Few data exist regarding sex differences of hemodynamic factors contributing to hypertension progression among untreated non-diabetic prehypertensive (PreHyp), Stage I and II subjects as define by JNC-7. With this in mind, we utilized non-invasive devises (BioZ.com, SonoSite Co, WA; SphymoCor, AtCor Medical, Australia; and Colin Medical Technology, Japan) to establish the hemodynamic characteristics of 104 hypertensive subjects (40 females) after a 4 week washout period from antihypertensive medications. Mean $\pm$ SD of the systolic (SBP) and diastolic (DBP), pulse pressure (PP), HR, stroke volume (SV), cardiac output (CO), systemic vascular resistance (SVR), and thoracic fluid content (TFC) were determined in subjects grouped into PreHyp (SBP, 131 $\pm$ 7 mmHg, n = 21) Stage I (SBP, 149 $\pm$ 6 mmHg, n = 49) and II (SBP, 172 $\pm$ 9 mm Hg n = 34). Despite there being no differences between females and males in terms of SBP, DBP and body mass index in each of the three hypertension categories, the increased blood pressure in PreHYP, Stage I and II males were characteristically associated with greater augmentations in SV and CO and lower SVR when compared to females (all $P < 0.05$). PP but not HR was lower in males compared to females across each of the three blood pressure categories while TFC was consistently higher in PreHYP, Stage I and II males. Brachial–ankle pulse wave velocity averaged 1718 $\pm$ 265 cm/s in females and 1.598 $\pm$ 289 cm/s in males ($P < 0.04$) while the augmentation index (AGM/PP) was markedly higher in hypertensive females (21.87 $\pm$ 7.74) compared to hypertensive males (13.76 $\pm$ 8.15, $P < 0.001$). The impact of sex differences in the hemodynamic factors accounting for the elevation in arterial pressure and its response to treatment has remained poorly characterized. This gap in knowledge may adversely influence choices of drug-treatment since our study shows for the first time that hemodynamics factors associated with increased blood pressure in women varied significantly for those accounting for high blood pressure in men.

Keywords: Prehypertension; Cardiac output; Vascular stiffness; Women

PO-18

IMPROVING GLOBAL VASCULAR RISK MANAGEMENT (GVRM) USING THE COSEHC™ CARDIOVASCULAR RISK ASSESSMENT TOOL

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The Consortium for Southeastern Hypertension Control (COSEHC™) developed a risk score tool to predict cardiovascular disease (CVD) mortality in the southeastern (SE) US. This global approach to SE CVD calculates the absolute risk for 5-year CVD mortality based on: age, sex, total, HDL and LDL-cholesterol, triglycerides (TG), SBP, and evidence of smoking, diabetes, family history of CHD, and ECG-confirmed cardiac hypertrophy. We now report on the goal rates for SBP, plasma lipid variables, and body mass index (BMI), based on published JNC-7 and ATP-III guidelines, from data available in the 2nd quarter (Q2) post-baseline of the GVRM Initiative; a 5-year project focusing on validating the COSEHC risk score through cardiovascular risk factor management. Baseline data were obtained from 78,540 patients (42 707 females) across ten medical facilities in FL (n = 2), NC (n = 1), MS (n = 1), SC (n = 4), and TN (n = 2). Results from 39 080 females and 33 144 males with Q2 data at goal for SBP (63 vs 70%), LDL-cholesterol (41 vs 55%), TG (59 vs 57%), and % of non-smokers were similar between the two sexes. Female subjects, however, achieved higher at goal targets for HDL-cholesterol (63 vs 36% in males, $P < 0.05$) and BMI (22 vs 16 in males, $P < 0.003$). In addition, at goal rates for SBP control correlated with improved HDL-cholesterol ($r = 0.64$, $P < 0.05$) and weight values in females ($r = -0.69$, $P < 0.05$) and only weight in males ($r = -0.76$, $P < 0.05$). COSEHC 5-year absolute risk scores for CVD mortality in the entire population were higher in males [(Mean $\pm$ SD) 36.43 $\pm$ 2.26] compared to females (30.57 $\pm$ 3.38, $P < 0.0005$). In summary, the GVRM

initiative provides an effective means of benchmarking risk factors in a population at high risk for cardiovascular events. The initiative is assisting health care providers to monitor risk factors at regular intervals and proactively manage the cardiovascular risk of their patient population.

Keywords: Cardiovascular risk factors; Essential hypertension; Stroke; Coronary heart disease.

PO-19

A COSEHC SPONSORED QUALITY IMPROVEMENT INITIATIVE ENRICHES CHRONIC DISEASE PRACTICE AND PERFORMANCE OF NORTH CAROLINA DIABETIC PATIENTS

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Recent studies showing considerable gaps in physician knowledge and application of cardiovascular disease (CVD) therapeutic recommendations led the Consortium for Southeastern Hypertension Control (COSEHC) to conduct physician continuous quality improvement (CQI) initiatives throughout the Southeastern United States to reduce the disproportionate CVD prevalence and mortality in the region. Cary Healthcare Associates, a North Carolina clinic, is currently one of 25 sites enrolled in COSEHC's ATGOAL (Aggressively Treating Global Cardio-metabolic Risk Factors to Reduce Cardiovascular Events) project. The ATGOAL project determines performance gaps from CVD variables from 300 random patients per site who have presented with ICD diagnosis codes of 250, 272, or 401. These de-identified patients are followed quarterly for 1 year as a way to measure changes in practice performance. Customized continuing medical education (CME) is provided by COSEHC faculty to address performance gaps using slides decks related to hypertension, hyperlipidemia, and glycemic control, patient expectations, physician-patient communication, and lifestyle/behavior modifications. At the first CME event, CVD care improvements are defined. At this first CME event, Cary Healthcare Associates decided to focus on diabetic patients and implemented the following system changes: (i) educate diabetic patients about the importance of blood pressure (BP) control; (ii) improve medication compliance by combining drugs, switching to generics, and addressing side effects; (iii) addressing clinical inertia; 4) educating providers about the importance of achieving BP goals especially among high risk populations. As a result of the ATGOAL interventions, there were improvements at first quarter in the percentage of diabetic patients at JNC7 systolic BP goals (<130 mm Hg), and ATP III LDL (<100 mg/dL) and HDL (>40 mg/dL) goals by 26%, 4%, and 4% respectively. These data demonstrate the effectiveness and the potential for CQI initiatives. In an attempt to address identified health disparities among different populations, the use of CME interventions designed for a specific provider can reduce CVD gaps and improve outcomes in high risk patients.

Keywords: Hypertension management; Diabetic patients; Physician quality improvement

PO-20

CARDIOVASCULAR CARE DISPARITIES IN A SOUTH CAROLINA PRIMARY CARE SITE PARTICIPATING IN THE COSEHC CUSTOMIZED MODEL OF INTERVENTION AND CARE (COSMIC) PROJECT

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This 18 month prospective nested cohort staggered design study will evaluate the effectiveness of a physician continuous quality improvement (CQI) program addressing gaps in physician application of cardiovascular disease (CVD) therapeutic guidelines called COSMIC [COSEHC Customized Model of Intervention and Care]. 2400 South Carolina primary care patients within one large medical practice were divided into two 1200 patient cohorts. The COSMIC intervention provided continuing medical education (CME) modules, systems changes, and the plan-do-check-act (PDCA) process of setting treatment and goal expectations with patients, promoting physician-patient relationship, lifestyle modifications, and evidence-based treatment algorithms followed by assessment of successes. One cohort has received baseline interventions. Cohort 1 had 75% of patients at systolic blood pressure (BP) goals (<140 mm Hg; <130 mm Hg diabetic), 51% at LDL cholesterol goals (<100 mg/dL), 68% at HDL cholesterol goals (>40 mg/dL) and an average HgA1c of $7.0 \pm 1.2\%$ for diabetic patients. While cohort 2 has not yet received any intervention, baseline assessment revealed that 65%, 50%, and 63% were at systolic BP, LDL cholesterol, and HDL cholesterol goals, respectively with diabetic patients having an average HgA1c of $6.8 \pm 1.2\%$. Disparities in care were greater in cohort 1 and 2 for diabetic and African Americans for systolic BP goals, females for LDL cholesterol goals, and diabetic patients for HDL cholesterol goals. While cohorts 1 and 2 possessed statistically similar baseline values for total cholesterol, LDL and HDL cholesterol, triglycerides, HgA1c, creatinine, and body mass index, cohort 1 had statistically lower systolic BP (131 ± 15 mm Hg vs 134 ± 17 mm Hg) and statistically higher diastolic BP (78 ± 9 mm Hg vs 77 ± 10 mm Hg) as compared to cohort 2. These data provide the basis for CVD CQI programs. Implementing CQI through the COSEHC/PDCA methodology may demonstrate significant improvements in CVD outcomes. This quality improvement process may be an effective method to improve health disparities within a patient population.

Keywords: Quality improvement; Cardiovascular disease; Hypertension; Disparities of care

PO-21

ADHERENCE TO COMPREHENSIVE INTERVENTIONS FOR MANAGEMENT OF UNCONTROLLED HYPERTENSION

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Home blood pressure (BP) monitoring has been advocated as a method for improving BP control, but there is little data on patients' long-term adherence. We describe adherence to home BP telemonitoring and telephone case management visits with a pharmacist. This analysis includes 160 patients with uncontrolled

BP enrolled in a randomized clinical trial who had completed 24 weeks of intensive intervention. They were asked to measure their BP a minimum of 6 times per week using a telemonitor that transmitted the readings via a modem to the case manager. Adherence to telemonitoring was defined as measuring ≥6 BPs/week for at least 17 (70%) of the 24 weeks. Across the 160 participants, the percentage of weeks with at least 6 readings taken ranged from 4% - 100% (mean 80%, median 88%, 25th percentile: 71%, 75th percentile 96%). 83% of participants had measured ≥6 BPs/week for at least 17 (70%) of the 24 weeks. Adherence was significantly higher in whites (85%) vs non-whites (66%) ($P = 0.04$) and in people age ≥65 (90%) vs <65 (77%) ($P = 0.03$, mean age was 64). Employment status was also significantly related to adherence ($P = 0.05$) with 77% adherence in those employed full time, 95% in those employed part time, 88% in retirees and 67% in the unemployed. Adherence did not vary significantly by gender ($P = 0.2$) or education ($P = 0.14$). In a multivariable analysis of these factors, older age was a significant independent predictor of adherence (OR 2.99, $P = 0.04$). The mean number of BP readings taken increased from month 1 (49) to month 2 (73), and then gradually decreased month 3–6, but still remained at recommended levels (66, 58, 50, and 40). Adherence to six mandatory phone visits with study pharmacists was also high, at 90.1% (865/960 visits complete), similar to adherence to the 6 month research clinic visit at 94% (151/160 visits completed). Despite an intensive visit and measurement schedule, adherence to BP telemonitoring was very high in the study population, and was maintained over 6 months. We conclude that this comprehensive intervention has the potential to improve BP control by conveying reliable blood pressure data to healthcare providers who can then close the feedback loop by making appropriate therapeutic adjustments.

Keywords: Adherence; Telemonitoring; Clinical trial.

PO-22

BLOOD PRESSURE CONTROL IN SPANISH SPEAKING PATIENTS WITH TYPE II DIABETES MELLITUS USING A GROUP VISIT MODEL

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Nationally there is a disparity in hypertension health outcomes in the Spanish speaking vs English speaking type II diabetes mellitus population.

To determine whether attending a group-based, four-part education program focusing on health literacy, will affect blood pressure control in Spanish speaking type II diabetes mellitus patients. We conducted a retrospective analysis of adult, Spanish-speaking patients (n = 134) with diabetes who attended a four-part, group-based program, which focused on health literacy, at an outlying general medicine clinic located in East Los Angeles. Clinical information such gender, HA1C, LDL, BMI, age, medication regimen, GFR, microalbuminuria, and presence of CAD was collected. We compared outcomes, using a paired T-test to evaluate the change in blood pressure from before to after attending the program.

Values of SBP for Spanish speaking patients before (mean, 139) and after (mean, 126) attending the sessions showed a SBP drop (absolute 13), 9.4% decrease in SBP.

Blood pressure control in Spanish speaking patients with type II DM can be achieved using a four-part, group-based education program that emphasizes health literacy.

Keywords: Spanish speaking; Hypertension; Latino; Diabetes mellitus

PO-23

A MULTI-LEVEL INTERVENTION TO CONTROL HYPERTENSION IN AFRICAN AMERICANS

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Hypertension-related outcomes explain the most mortality gap between African Americans and whites. Despite effective blood pressure (BP) control interventions, these approaches have not been translated into clinical practice for hypertensive African Americans. This study evaluated the effectiveness of a multilevel evidence-based intervention [targeted at physicians and patients] in improving BP control in hypertensive African Americans in 30 community health centers (CHCs). Counseling African Americans to Control Hypertension (CAATCH), a cluster randomized clinical trial, compared an Intervention (IC, n = 15) consisting of three patient-level components (interactive computerized hypertension education, home BP monitoring, monthly lifestyle modification counseling) and two clinician-level components (monthly Hypertension Guidelines (JNC-7) case rounds, chart audits/feedback) with Usual Care (UC, n = 15). The primary outcome was the rate of BP control (BP < 140/90 for all patients; or <130/80 for diabetic patients) at 12 months by automated BP monitor (BPTru BPM-300). Secondary outcome was Office BP (extracted from medical records) at 12 months. Of 1059 recruited, 71% completed the trial (mean age 56 years, 60% obese, 35% diabetes, baseline BP (+SD) 149/90 (+21/13 mmHg). Using intent-to-treat analysis, BP control at 12 months by BPTru (adjusted for baseline BP, diabetes, Charlson comorbidity, resistant hypertension) was IC = 59.9% vs UC = 55.1% [OR = 1.22 (95%CI 0.95–1.57)]; and mean Office BP at 12 months was IC = 135.4 mmHg vs UC = 141 mmHg ($P < 0.01$). In pre-specified subgroup analyses, the intervention was associated with greater BP control for patients without diabetes [IC = 61.6% vs UC = 53.6%, OR = 1.39 (1.02–1.9)]; and patients who received care in small CHCs [IC = 62.5% vs UC = 52.2%, OR = 1.53 (1.08–2.15)]. In African Americans with poorly controlled hypertension, while a practice-based multilevel intervention did not significantly improve BP control by BPTru, it was associated with significant improvement in Office BP; thus suggesting that BP targets can be reached in this high-risk population. Our findings suggest that evidence-based multilevel interventions can be integrated into primary care practices with significant potential for improving BP control in hypertensive African Americans.

Keywords: Home blood pressure monitoring; Multilevel intervention; African Americans; Hypertension control

PO-24

BARRIERS TO SELF-EFFICACY AMONGST RACIALLY SIMILAR BUT ETHNICALLY DIVERGENT EMERGENCY DEPARTMENT PATIENTS WITH HYPERTENSION

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Background: Among those with chronic hypertension (cHTN), blood pressure (BP) control is far worse when perceived

self-efficacy for disease management is low. Emergency department (ED) patients with cHTN are at-risk for poor BP control but little is known about self-efficacy in this group.

Objectives: (1) To evaluate perceived self-efficacy for medication adherence in ED patients with cHTN; and (2) to compare identifiable barriers among racially similar but ethically divergent subgroups.

Methods: A validated, 25-item medication adherence self-efficacy scale (MASES) was administered to ED patients of African origin with cHTN at three locations: Detroit Receiving Hospital (DRH - Detroit, MI), the Tanzanian Training Center for International Health (TTCIH - Ifakara, TZ) and University Hospital of the West Indies (UHWI - Kingston, JA). Responses to the scale along with demographic and basic clinical data were collected and multilevel comparisons were performed using Kruskal–Wallis or ANOVA tests, where appropriate.

Results: One hundred and ninety-seven patients were enrolled (97 at DRH, 50 at TTCIH, and 50 at UHWI). MASES responses showed poor self-efficacy overall with 33.7% (n = 67) of the cohort certain of compliance to a lifelong regimen. Only 45.2% (n = 89) were certain they could take their BP medications if they were expensive. 51.2% (n = 101) were certain about medication adherence in the face of side-effects. Increased cost had greatest effect on self-efficacy at DRH (29.9% certainty of compliance vs 52% at TTCIH, and 68% at UHWI; $P < 0.001$). Only 38% of UHWI respondents were certain they could take their medications if they cause sexual dysfunction (vs 63% at DRH and 62% at TTCHI; $P = 0.03$).

Conclusions: In this racially similar but ethnically divergent cohort of hypertensive ED patients, cost and concern over side-effects were important barriers to medication self-efficacy, particularly in those recruited at DRH and UHWI, respectively.

Keywords: Self-efficacy; Hypertension; African.

PO-25

PHYSICAL CHARACTERISTICS OF SALT IN THE TREATMENT AND PREVENTION OF HYPERTENSION

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This study analyzed the physical characteristics of commonly used salts to determine their potential impact in the treatment and prevention of hypertension. The volume, density, mass, and crystal structure was analyzed in the following salts: Diamond Crystal Iodized Salt (Salt Sense), Meijer Iodized Free Flowing Salt, Morton Iodized Salt and Morton Coarse Kosher Salt. The mass and density was calculated from 10 measurements from each salt weighed separately. The length and crystal structure of each salt was determined using an ocular lens on a light microscope, measuring four grains of salt from each different type of salt.

The DASH Diet recommends 1.5 g of sodium a day; the density of each salt was used to calculate the tsps of salt containing 1.5 g of sodium. The results for mass, density and tsps of salt containing 1.5 g of sodium are shown in the table below.

These results show that Salt Sense has a lower density, lower mass, and more salt per 1.5 g by volume of sodium as compared to other store bought brands of salt. This study demonstrates that Salt Sense could allow patients to eat "salty" food while still lowering their sodium intake. This has potential implications for the non-pharmacological treatment and prevention of hypertension.

Physical Characteristics of Salt in the Treatment and Prevention of Hypertension

	Salt Sense	Meijer Iodized Salt	Morton Iodized Salt	Coarse Kosher Salt
Mass (g) in 10 mL vol	7.48 ± 0.148	13.16 ± 0.295	12.6 ± 0.205	9.69 ± 0.202
Density g/mL	0.748 ± 0.014	1.316 ± 0.028	0.298 ± 0.0194	0.387 ± 0.0192
Tsp of salt in 1.5 g sodium	1.002	0.57	0.596	0.774
Length of salt crystals in mm	0.5 ± 0.038	0.5 ± 0.077	0.3 ± 0.074	1.2 ± 0.247

Keywords: Dietary treatment of hypertension; Dietary prevention of hypertension; Physical characteristics of salt; Salt.

PO-26

RELATION BETWEEN CARDIOVASCULAR RISK SCORE, ASYMPTOMATIC PERIPHERAL DISEASE AND LEFT VENTRICULAR HYPERTROPHY

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Objectives: To determinate the relation between cardiovascular risk (CVR) measured by Score, the presence of peripheral arterial disease (PAD) (ankle brachial index (ABI) <0.9) and left ventricular hypertrophy (LVH) measured by electrocardiographic criteria in patients hospitalized into an Internal Medicine Service.

Method: A transversal and non-interventional trial was carried out in hospitalized patients into an Internal Medicine Service of two hospitals at Valencia (Spain), during a 3-months period. Patients were selected according to the age, sex and CVR factors such a smoking, high blood pressure, diabetes mellitus, lipid disorders and cardiovascular precedents. The presence of PAD was determined by measuring the ABI; PAD was considered present when the ABI was <0.90. Cornell and Sokolow-Lyon voltage indexes were determined as an ECG criteria.

Results: Of 150 clinical checked histories, we observed:

Conclusions: PAD, especially in the asymptomatic stage is common, and its prompt screening and treatment can reduce CVR. ABI is the most cost-effective tool for lower extremity PAD detection and provides objective data both for the diagnosis in epidemiological surveys and in-office practice, and monitoring of efficacy of therapeutic interventions. Since it can be predicted the major percentage of determinations of HVI and ABI < 0.9 it is observed in patients with high and very high CVR (25.1% and 37.81% respectively). Nevertheless, in this group of patients this finding does not modify the prevention risk level or therapeutics attitude to continuing, for what his accomplishment loses interest. On the other hand a high percentage of ITB is estimated <0.9 (21.42%) in the group of patients by moderate CVR. It is in this group where the mentioned determination assigns these individuals to the secondary prevention risk level and exchange the therapeutic attitude. LVH determination seems to be less effective for the group of moderate CVR, since it proved to be positive in only 14.28% of the cases.

Table I.

ABI	Patients with LVH	Patients without LVH	Score
<0.9	8	17	Very high risk
0.9–1.2	0	15	Very high risk
>1.2	2	6	Very high risk
<0.9	9	11	High risk
0.9–1.2	10	29	High risk
>1.2	0	12	High risk
<0.9	2	4	Moderate risk
0.9–1.2	2	16	Moderate risk
>1.2	0	4	Moderate risk

Mean age was 75.95 years (SD 12.15).

Keywords: Score; Asymptomatic peripheral disease; Left ventricular hypertrophy; Ankle brachial index

PO-27

A COMPUTER-MEDIATED INTERVENTION AND DASH DIET, WHEELS-I PROGRAM, SUSTAINS IMPROVED BLOOD PRESSURE OVER 8 WEEKS IN WOMEN FROM DIVERSE ETHNIC BACKGROUNDS

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Background: The Dietary Approaches to Stop Hypertension Diet (DASH) can promote healthier eating habits and reduce uncontrolled blood pressure (BP), especially in African Americans. Adherence to DASH portion controlled eating pattern is a difficult lifestyle change, and effective implementation and follow-up in clinical practice requires time, staff, and resources.

Objective: This study examines whether a new innovation, a self sustaining personalized computer-mediated information system involving DASH and a cognitive-behavioral intervention (CBI) improves BP and weight loss in women with Stages 1 and 2 hypertension.

Methods: This clinical trial was conducted with 70 women (74% African American, ages 35–76) seen at outpatient clinics and randomly assigned to experimental (CBI) or control groups (CG). The CBI group was exposed to email messages, 28 morning, and 56 evening, linked to web-based rapid response surveys designed to document both momentary assessment and momentary performance of DASH self-care activities.

Results: No significant differences were found in the clinic SBP baseline measures (mean, 136 mmHg (SD = 17.71) between the CBI and CG. Repeated measures ANOVA with SBP measures by group-no sphericity assumption violation-demonstrated the mean scores at baseline, 1 and 3 months post intervention were statistically significantly different ($F(4.585, 2) = 510.229$, $P = 0.012$). For CBI group, paired T-test for SBP at 1 and 3 months were significantly different ($P = 0.000$ and $P = 0.004$), -9.1 mmHg (SD = 14.66) and -8.22 (SD = 16.80) compared to 2.26 (SD = 15.23) and -.40 (SD = 13.14) for CG. Women in CBI with baseline SBP >140/90 showed SBP mmHg reductions of -13.09 (SD = 12.89) and -13.04 (SD = 13.04) at 1 and 3 months. No significant differences were revealed between groups for weight loss; modest reductions of -1.1 and -1.4 pounds were shown for CBI compared to -.76 and -.86 for CG.

Conclusions: The study showed an effective approach for advancing BP control with evidence-based research, methodology, and technology. Further study will benefit African American women who are at great risk for cardiovascular disease due to uncontrolled BP.

Keywords: Computer-mediated cognitive behavioral intervention; DASH diet; Blood pressure control; Lifestyle modification

PO-28

RELATIONSHIPS BETWEEN AGGRESSIVE SYSTOLIC BP GOALS, NOCTURNAL BP DIPPING, AND CAROTID ATHEROSCLEROSIS IN TYPE 2 DIABETES: THE SANDS STUDY

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Aggressive SBP and LDL-cholesterol (LDL-C) goals reduced carotid intima medial thickness (CIMT) and led to a greater decrease in left ventricular (LV) mass than standard goals in patients with type 2 diabetes in the Stop Atherosclerosis in Native Diabetics Study (SANDS). Although CIMT and LV mass have been related to nocturnal BP dipping in patients with essential hypertension, it is unclear whether lower BP goals increase nocturnal dipping as assessed by 24-hour ambulatory BP monitoring.

We performed 24-hour BP monitoring in a subset of SANDS participants (N = 156, 75 assigned to the aggressive [115 mm Hg SBP] goal and 81 assigned to the standard [130 mm Hg] goal) on stable antihypertensive therapy during the third (final) study year to evaluate relations between BP goals, nocturnal BP dipping, and CIMT and LV mass. Dipping was defined as a decline in mean SBP > 10% from waking to sleep. After having the patient sit for 5 minutes, the initial 24-hour BP reading was used as office BP.

Mean office and 24-hour BP readings differed significantly between treatment groups, but no differences were observed in prevalence of nocturnal dipping (Table). No statistically significant relationships were observed among baseline CIMT, LV mass, and BP dipping (two-sample *t*-tests). Linear regression models showed that BP dipping did not independently predict changes in CIMT or LV mass.

Targeted office BP goals were not correlated with nocturnal BP dipping. Dipping status in these actively treated patients did not independently predict CIMT or LV mass outcomes beyond targeted office SBP goals.

BP Characteristics by Treatment Group

	Aggressive N = 75 Mean (SD)	Standard N = 81 Mean (SD)	*P*-value
Office SBP*	122 (12)	132 (16)	<0.001
Office DBP	66 (10)	73 (11)	<0.001
Ambulatory BP			
24-hour SBP	116 (12)	123 (13)	<0.001
24-hour DBP	60 (7)	66 (8)	<0.001
SBP awake	120 (11)	128 (13)	<0.001
SBP asleep	112 (14)	119 (14)	0.004
DBP awake	63 (8)	69 (9)	<0.001
DBP asleep	57 (8)	63 (9)	<0.001
SBP dippers N (%)	25 (33)	28 (35)	0.87**

*BP values are in mm Hg. ** Based on chi-square test.

Keywords: Nocturnal blood pressure dipping; Blood pressure goals; Carotid atheroscerlosis

PO-29

IMPROVED HYPERTENSION CONTROL RATES THROUGH A MULTIDISCIPLINARY REGIONAL APPROACH

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Objective: In December of 2007 Kaiser Permanente Colorado had a regional hypertension (HTN) control rate of 61%. In response to this analysis better hypertension control became a regional Primary Care quality initiative.

Methods: Four interventions were launched from 2008–2010 focusing on improved efficiency of the Primary Care teams and removal of member perceived barriers (i) Provision of no co-payment walk in or scheduled nurse visit blood pressure checks (ii) Collaboration with Clinical Pharmacy Specialists in the primary care clinics to manage blood pressure medications per the HTN Collaborative Drug Therapy Management (CDTM) protocol. (iii) Implementation of regional systemic medical record reviews and outreach to patients with persistently elevated blood pressure (iv) Development of a blood pressure alert at all outpatient facilities prompting nursing staff to repeat an elevated blood pressure if indicated.

Regional, medical office and provider level quality hypertension dashboards were developed to allow tracking of progress over time. Dashboards were made visible on the intranet to all providers and staff with monthly updates. Concurrently, nursing dashboards were adopted measuring nursing staff compliance with the blood pressure alert.

Results: As a result of these interventions the hypertension control rate for members age 18–85 has increased from 61% in January of 2008 to 78% in November of 2010.

Conclusion: After the development of these various multidisciplinary regional efforts the Kaiser Permanente Colorado hypertension control rate improved from 61% to 78% over a three year period. Strong sponsorship with accountability were important contributors to success and many of these interventions can be implements in multiple health care settings.

Keywords: Hypertension; Multidisciplinary regional efforts; Blood pressure alert; Systemic medical record review

PO-30

CLINICAL PHARMACIST-PHYSICIAN TEAM APPROACH IN TREATING RESISTANT HYPERTENSION CASES

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Patients with resistant hypertension pose a special challenge when they have multiple comorbidities, medication intolerances, and are seen by different providers. At Kaiser Permanente, a strategy was set in place to identify and treat resistant hypertensive patients utilizing a Clinical Pharmacist-Physician Hypertension Specialist team approach. Cases were submitted by Clinical Pharmacists from the Diabetes/Cardiovascular Disease, Heart Failure, Medication Therapy Management, and Nephrology Services. Twenty five patients, garnered March to June 2010, were evaluated at monthly meetings. Treatment strategies were developed to move patients towards blood pressure goal or maintain those already at goal by streamlining drug regimens. Patients were receiving an average of 5.3 antihypertensives and mean blood pressure was 148/70 at baseline. Successful strategies were to rechallenge medications at low doses based on questionable or dose-related intolerances, optimize thiazide use and other drug classes for compelling indications, lower pill counts by stopping duplicate medications and consolidating doses. The Clinical Pharmacist who submitted each case implemented the changes, provided medication counseling, ordered repeat labs, and followed the blood pressure course. For ten cases, the treatment recommendations were electronically routed to the patient's Primary Care Physician, Cardiologist, or Nephrologist. Four patients were referred to see a Physician Hypertension Specialist in clinic. Sixteen out of twenty five cases (64%) had all or part of the treatment recommendations implemented. In these sixteen patients, eight (50%) moved from uncontrolled to goal blood pressure of <140/90 mm Hg; four (25%) maintained goal blood pressure after their regimens were streamlined; one (6%) saw blood pressure trending closer to goal; three (19%) did not show improvement. Thiazides were optimized in four patients, drugs for compelling indications initiated for three patients, medication intolerances successfully rechallenged in three patients, and pill count per day was reduced from 9.8 to 8.6. Overall, the Clinical Pharmacist–Physician Hypertension Specialist designed regimens facilitated improvement in most of the patients by optimizing and simplifying complex drug regimens.

Keywords: Resistant hypertension; Clinical pharmacist; Hypertension specialist

Endothelial Function

PO-31

A NOVEL ANP-LIKE PEPTIDE, ANP1-28RR, REVEALED BY A SINGLE NUCLEOTIDE POLYMORPHISM OF THE ANP GENE, RS5065 FOR A PEPTIDE WITH INCREASED PERMEABILITY PROPERTIES *IN VITRO*

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Atrial natriuretic peptide (ANP), a blood pressure lowering cardiac peptide, is a 28-amino-acid peptide synthesized and secreted by the heart which possesses cardiorenal protective properties mediated by the second messenger cGMP. Recent human genetic studies have revealed that the minor C-allele of rs5065, a single nucleotide polymorphism (SNP) of the ANP gene, encodes an ANP1-28 with two additional arginines at the carboxyl terminus (ANP1-28RR). Importantly, in the ALLHAT study this ANP gene variant was associated with modification of anti-hypertensive effects of cardiovascular disease and blood pressure. Historically, natriuretic peptides with modifications, which lengthen the C-terminus, have shown greater resistance to enzyme degradation. In addition, changes to the C-terminus could affect receptor binding as well as affinity. In our study, we sought to assess and compare native ANP1-28 and ANP1-28RR biological actions on both cGMP generation in human cultured cardiac fibroblasts, and on cell permeability in human aortic endothelial cells. We evaluated the ability of three different equimolar concentrations of ANP1-28 and ANP1-28RR (10^{-10} mol/L, 10^{-8} mol/L, 10^{-6} mol/L) to stimulate cGMP production. At the highest concentration ANP1-28RR demonstrated a trend for greater cGMP production (0.72 vs 0.45 pmol/mL, $P = 0.080$), approaching statistical significance. Secondly, when assessing endothelial cells permeability, all three concentrations of this novel peptide ANP 1-28RR significantly enhanced human aortic endothelial cell

permeability (69 vs 29 RFUs, $P = 0.012$; 58 vs 39 RFUs, $P = 0.015$; 58 vs 32 RFUs, $P = 0.059$) compared to native ANP1-28. In summary, these findings establish that the addition of two arginine to the C-terminus of native ANP1-28 enhances the biological action of ANP1-28 in vitro in the generation of cGMP and especially in the regulation of endothelial permeability. Further studies are warranted to define actions in vivo of ANP1-28RR and to evaluate the therapeutic potential of this novel ANP peptide revealed by genomic medicine.

Keywords: Atrial natriuretic peptide; Natriuretic peptides; Endothelial permeability; cGMP

PO-32

EXAGGERATED EXERCISE BLOOD PRESSURE RESPONSE IS ASSOCIATED WITH ARTERIAL STIFFNESS, ASYMMETRIC DIMETHYLARGININE AND OSTEOPROTEGERIN IN ESSENTIAL HYPERTENSION

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A hypertensive response to exercise (HRE) is associated with high cardiovascular risk, while elevated levels of asymmetric dimethylarginine (ADMA) and osteoprotegerin (OPG) are related to atherosclerosis progression. In this study we sought to determine the relationships of HRE with ADMA, OPG and arterial stiffness in hypertensives.

Our population of 240 newly diagnosed never treated non-diabetics with stage I to II essential hypertension [155 men, mean age = 51 years, office blood pressure (BP) = 150/96 mmHg] with a negative treadmill exercise test (Bruce protocol) was divided into those with HRE (n = 70) (peak exercise systolic BP ^{3}210 mm Hg in men and ^{3}190 mm Hg in women) and those without HRE (n = 170). Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV) values. Patients with HRE compared to those without HRE had greater 24-hour systolic BP (143 ± 9 vs 131 ± 8 mm Hg, $P < 0.05$), while did not differ regarding metabolic profile and left ventricular mass index (P = NS). Patients with HRE as compared to those without HRE exhibited greater levels of ADMA (0.63 ± 0.04 vs 0.52 ± 0.05 μmol/L, $P < 0.0001$), OPG (5.4 ± 0.1 vs 4.1 ± 0.5 pmol/L, $P < 0.0001$) and PWV (8.9 ± 1.7 vs 7.5 ± 0.9 m/s, $P < 0.0001$), independently of confounders. In the total population, peak exercise systolic BP was related to 24-hour systolic BP ($r = 0.249$, $P < 0.05$), PWV ($r = 0.278$, $P = 0.003$), ADMA ($r = 0.260$, $P = 0.007$) and OPG ($r = 0.214$, $P < 0.05$). Regarding OPG, it was associated with 24-hour systolic BP ($r = 0.285$, $P < 0.0001$), ADMA ($r = 0.284$, $P < 0.05$) and PWV ($r = 0.424$, $P < 0.0001$). Multiple regression analysis showed that 24-hour systolic BP ($b = 0.216$, $P = 0.003$), male sex ($b = 0.270$, $P < 0.05$), ADMA ($b = 0.225$, $P = 0.006$) and OPG ($b = 0.188$, $P < 0.05$) were independent predictors of peak exercise systolic BP.

In essential hypertension, a HRE is accompanied by a state of increased arterial stiffening, endothelial dysregulation and progressive atherosclerosis. The interrelationships of ADMA and OPG with exercise BP response and stiffness support that diffuse vascular dysfunction contributes to HRE-related risk in hypertension.

Keywords: Exercise testing; Endothelial dysfunction; Arterial stiffness; Atherosclerosis

PO-33

ENDOTHELIAL IMPACT OF BLOOD PRESSURE ABOVE THE GOALS IN HYPERTENSIVE PATIENTS

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Background: According to Quality and Outcomes Framework (QOF) at least 70% of patients should be within the goals of blood pressure. These goals are set based on mobility and mortality but a question remains: are they correlated with the degree of inflammation and endothelial dysfunction? AIMS: To study inflammation and endothelial dysfunction in hypertensive patients in order to assess the real impact of achieving the blood pressure goals.

Methods: N = 127 hypertensive, 64.2 (11.6) years, 31–85 years, 52% males, 28% with prediabetes, 47% type 2DM, 13% with coronary heart disease (CHD) and 21% smokers. Blood pressure goals: in non-diabetics: <140/90 mmHg; t2DM: <= 130/80 mmHg. LDL-c goals: isolated hypertension <115 mg/dL; hypertension+T2DM<100; hypertension+CHD <70. The population was divided into two groups according to goals. Both groups presented similar age, LDL-cholesterol, diabetic status and HbA1c. BMI (kg/m^2) and waist (cm). Blood pressure (OMRON 705). Biochemical parameters: Hitachi autoanalyzer. HbA1c: (%) HPCL. ADMA (μmol/l) ELISA DLD. NEOPTERIN (ng/mL).ELISA DRG. s-TNF-R(80 kDa)(ng/mL): ELISA eBioscience. Statistical: Mean (SD). Normality by Kolmogorov–Smirnov test. Comparison between groups by Student-*t* test or Mann–Whitney-*U* test as appropriate. Chi-square test.

Results: 1. 40% of hypertensive patients were below the BP target, whereas 57% achieved LDL-c goals. 2. Patients above blood pressure goals presented higher neopterin values: 2.33 (0.73) vs 2.09 (1.26); $P = 0.037$. 3. The same group of patients was also found to have higher sTNF-R: 24.2 (10.2) vs 20.4 (10.4), $P = 0.038$)) 4. With regard to direct endothelial damage, ADMA levels were increased in non-controlled blood pressure patients: 0.45 (0.07) vs 0.40 (0.07) $P = 0.039$. 5. In our study no significant differences were observed in CRP between both groups.

Conclusions1. Non-controlled blood pressure is a marker of vascular inflammation and above all, a marker of endothelial dysfunction.

2. According to our results, in a scientific community focused on cholesterol, a good blood pressure control is "a must" if we want to brake the atherothrombotic disease. 3- Take-home suggestion: We need to dive into the vascular endothelium beyond CRP assay, a non-specific biomarker.

Keywords: Blood pressure; Inflammation; Endothelial dysfunction

PO-34

PLASMA SODIUM BUT NOT SODIUM TO POTASSIUM RATIO COULD BE A SIMPLE AND LOW-COST TECHNIQUE TO PREDICT VASCULAR INFLAMMATION. CORRELATION WITH RESISTIN LEVELS

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Background: The 2010 US dietary guidelines recommend consumption of potassium-rich foods as well as consumption of little

salt. The urinary sodium-to-potassium excretion ratio predicts the risk of cardiovascular disease better than sodium or potassium excretion alone. The impact of plasma sodium and sodium/potassium ratio has not been researched. Aims: To evaluate if plasma sodium and/or sodium to potassium ratio could predict inflammation (resistin) and endothelial dysfunction (ADMA) Methods N = 236, 58.2 (13.6) years, 53% males, 64% hypertension, 34% type2 DM and 20% smokers. Those values out of normal range for Na and K were excluded. BMI (kg/m^2) and waist circumference (cm).Glycemia, creatinine, HDL-cholesterol, LDL-cholesterol, total cholesterol and triglycerides, assessed by Hitachi autoanalyzer. The population was divided into terciles according to Na: Cut-off points (<139;>142). According to Na/K ratio: Cut-off points (33.8; 36.4). Average age was similar in both groups. Blood pressure (OMRON 705 CP): systolic and diastolic blood pressures (SBP and DBP) and heart rate (HR)]. Plasma renin activity (ng/mL/h) RIA Immunotech. ADMA (μmol/l): EIA DLDStatistical analysis: Mean (SD). Kolmogorov–Smirnov test.. Student-*t* test or Mann-Whitney-U test as appropriate.

Results: 1.- Patients in the upper tercile of Na presented higher resistin values: 3.61 (3.3) vs 2.54 (1.79); $P = 0.04$) than those in the lower tercile. 2. No significant differences were found between both groups in ADMA values. Three Patients in the upper tercile of Na/K ratio presented equivalent values of resistin and ADMA.

Conclusions: Plasma sodiun together with glucose, HbA1c, LDL-C, HDL-C, and TGs could full a cardiometabolic portray that engages by its low-cost. Its relation with resistin levels suggests an attractive pathogenic mechanism. Now we have a new reason to curb the salt intake of ours patients.

Keywords: Plasma sodium; Resistin; Endothelial dysfuntion

PO-35

TIME FOR ACTION. CORRELATION BETWEEN PLASMA RENIN ACTIVITY AND BIOMARKERS. A MANDATORY STUDY AS RESULT OF A RECENT HEART OUTCOMES PREVENTION EVALUATION ANALYSIS

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The global management of hypertensive patients is undergoing a constant re-engineering. In HOPE, patients with elevated levels of plasma renin activity (PRA) at baseline were at increased risk of cardiovascular death. The association persisted after adjustment for multiple risk factors, including C-reactive protein (CRP).

Aims: To study if higher levels of PRA are associated with oxidative stress (total antioxidant capacity (TAC) and superoxide dismutase (SOD)) and endothelial dysfunction (VCAM-1) in a population with moderate-high cardiovascular risk.

Methods: N = 112, 57.5 (14.8) years, 50% males, 63% hypertension, 31% type 2DM; 6% with coronary heart disease and 21% smokers. The population was divided into terciles according to PRA levels: Cut-off points: [0.48; 1.35]; BMI (kg/m^2) and waist circumference (cm). Blood pressure (OMRON 705 CP): systolic and diastolic blood pressures (SBP and DBP) and heart rate (HR)]. Glycemia, creatinine, HDL-cholesterol, LDL-cholesterol, total cholesterol and triglycerides, assessed by Hitachi autoanalyzer. SOD (U/mL) Colorimetric assay. Cayman. VCAM-1 (ng/mL) EIA. Bender Medsystems. (Nm). Colorimetric assay. Cayman. Plasma renin activity (ng/mL/h) RIA Immunotech. Statistical analysis: Mean (SD). Kolmogorov–Smirnov test. Student-*t* test or Mann–Whitney-*U* test as appropriate.

Results: Patients in the upper tercile of PRA presented higher VCAM-1 values: ($P = 0.041$) and lower SOD values ($P = 0.004$) and TAC ($P = 0.001$). Those patients with hypertension showed higher PRA values ($P = 0.005$). 4- Hypertensives within the upper tercile of PRA presented equivalent SBP and DBP values than those in lower tercile.

Conclusions: 1. High PRA levels may be responsible for activating endothelial dysfunction and oxidative stress, particularly through mechanisms involving VCAM-1, SOD and TAC.
2. According to our results, PRA is a proinflammatory biomarker and an active participant in atherothrombotic disease.
3. To evaluate PRA in moderate-high CV risk is a "fast track" to know the proinflammatory status as a complement to CRP.

Keywords: Plasma renin activity; Superoxide dismutase; Proinflamamatory biomarker

PO-37

VARIABILITY OF FLOW MEDIATED DILATION TECHNIQUE: A MULTICENTRE ITALIAN STUDY

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Objective: Endothelial dysfunction is recognized as a key mechanism in the patho-physiology of atherosclerosis. Flow-mediated dilation (FMD) of the brachial artery is the most widely used method for assessing endothelium-dependent vasodilation since it is not invasive and its impairment has been shown to be predictive of cardiovascular events. Despite this, some challenges might limit FMD assessment, including its variability and operator dependency. The aim of this study was to evaluate the variability of FMD assessment in a multicenter setting with standardized procedures.

Methods: One hundred and thirty-five healthy volunteers (20–60 years) from six Italian Hypertension Units were included into the study. FMD was assessed as dilation of the brachial artery secondary to 5 min wrist ischemia. Ultrasound images of the brachial artery were VCR recorded for baseline FMD (time 0) and repeated 1 hour after (time 1). A third sequence was obtained 1 month apart (time 2). Endothelium independent vasodilation to GTN was also evaluated at time 1 and 2. FMD and response to GTN changes were measured blindly as percentage changes in brachial artery diameter by an automatic edge detection system (FMD Studio, IFC-CNR, Pisa, Italy). The intra/inter-session coefficients of variation were calculated to assess FMD and GTN variability over time.

Results: All recordings were suitable for analysis. FMD was $6.50 \pm 3.01\%$ at time 0, $6.34 \pm 3.09\%$ at time 1 and $6.42 \pm 2.97\%$ at time 2. Overall, the intra-session FMD coefficient of variation was $9.4 \pm 10.6\%$. Inter-session FMD coefficient of variation was $14.8 \pm 11.9\%$. Endothelium-independent vasodilation to GTN was 12.2 ± 5.2 and $12.4 \pm 4.9\%$ at time 1 and 2, respectively. The overall inter-session coefficient of variation of GTN response between assessments obtained at time 1 and time 2 was $16.2 \pm 11.3\%$.

Conclusions: This study show a good reproducibility of FMD assessment over time in a population of healthy subjects. At variance with the debated poor reproducibility of the technique and its high operator dependency, results show a similar coefficient of variation for intra/inter-session FMD assessment, suggesting that a rigorous and standardized procedure ensures an adequate reproducibility over time for FMD in multicenter studies and in future clinical trials.

Keywords: FMD; Endothelial function

PO-38

ENDOTHELIAL DYSFUNCTION IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME

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Objectives: To study the possible relationship between glucose abnormalities and endothelial function, and their possible relationship with adipokine markers in patients with hypertension and metabolic syndrome (MS).

Methods: We studied 28 hypertensive patients with MS, according to NCEP-ATPIII criteria. IR was estimated by HOMA index. According to OGTT (75 g), we divided into two groups: Patients with normal glucose tolerance (Fasting glucose <100 mg/dL and 2 hour glucose <140 mg/dL) (NG group = 8 patients) and patients with abnormal glucose tolerance (nine subjects with glucose intolerance and 11 patients with type 2 diabetes). The endothelial dysfunction was evaluated by brachial artery ultrasonographic (Echo Blaster 128; transductor 7.5 MHz), endothelial dependent-vasodilation(EDVD) was measured during reactive hyperaemia (%change in the diameter of brachial artery after 1 min of hyperaemia). The endothelial independent-vasodilation (EIVD) was measured by the nitroglycerin (0.4 mg sublingually) administrated after at least 10 minutes of rest following reactive hyperemia. The maximum vasodilation occurs three to four minutes after administration. Adiponectin levels were measured by RIA.

Results: AG patients had more insulin resistance tan subjects in NG group. Moreover, AG subjects were elderly (67.2 ± 4.5 vs 46.8 ± 5.6; $P < 0.05$), and lower adiponectin levels ($P < 0.05$). The percentages of change in EDVD and EIVD were: 19.54 ± 12.5 years 6.68 ± 5.2, respectively. In AG group (n = 20), the percentage of change in EDVD was lower (10.1 ± 6.2) than NG group (29.34 ± 15). Any relationship between insulin resistance and endothelial dysfunction was found ($r = -0.12$ year -0.009; P = NS, respectively). Adiponectin levels (6.64 ± 4.5 μg/mL) showed a significant relation with insulin resistance ($r = 0.59$; $P < 0.05$). We did not find any significant correlation between adiponectin and EDVD or EIVD ($r = -0.01$; P = NS).

Conclusions: The glucose metabolism abnormalities in hypertensive patients with metabolic syndrome are related to elderly, lower adiponectin levels and lower vascular reactivity (estimated by EDVD).Although we did not find any significant association between endothelial dysfunction and insulin resistance or adiponectin levels, more studies with a larger sample of patients will be necessary to confirm these outcomes.

Keywords: Endothelial; Glucose; Adiponectine; Metabolic syndrome

PO-39

NORMATIVE BRACHIAL ARTERY DIAMETER DILATATION FOLLOWING REACTIVE HYPEREMIA

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The purpose of this study was to establish normative data for the percent of change in the brachial artery diameter following reactive hyperemia in healthy subjects using ultrasonography.

Flow-mediated dilatation (FMD) was assessed in 47 healthy subjects (29 men, 18 women) between the ages of 20–46 with a mean age of 25.9 ± 5.3. The diameter of the brachial artery was measured from intima to intima on longitudinal sonographic images (GE LOGIQ *e*, GE Healthcare, Milwaukee, WI). Images were obtained proximal to the superior aspect of a blood pressure cuff on the right arm. Three brachial artery diameter measurements were taken immediately before and after a 5 min interruption of the brachial artery flow. FMD was expressed as the percent relative change from baseline.

In the healthy subjects, the mean ± standard deviation for the FMD was 6.9% ± 4.9 (range, -2.2 to 16.3%). Pre and post measurement values of the brachial artery diameter were significant ($P < 0.05$).

This study presents normative FMD of the brachial artery diameter following reactive hyperemia. This data will be used in future studies designed to assess the effect of a clinical intervention on flow mediated dilatation.

Keywords: Ultrasonography; Brachial artery; Vasodilation; Endothelium, vascular

PO-40

SEVERITY OF OBSTRUCTIVE SLEEP APNEA AND ATHEROSCLEROSIS: MULTIPLE ASSOCIATIONS IN THE SETTING OF HYPERTENSION

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We investigated the effect of obstructive sleep apnea (OSA) on the levels of diverse indexes of an atherogenic substrate in a hypertensive population.

87 subjects with stage I-II untreated essential hypertension and OSA (apnea-hypopnea index-AHI >5) diagnosed with polysomnography (PSG) (aged 48 ± 7 years, office BP 151 ± 6/97 ± 8.4 mmHg) and a control group of 96 hypertensive patients without OSA (negative PSG) matched for age, gender, BMI and smoking habits were studied. All subjects underwent ambulatory blood pressure monitoring, echocardiography and carotid-femoral pulse wave velocity (c-f PWV) measurement with an automated device (Complior SP). Morning blood samples were collected for routine laboratory testing and for estimation of levels of asymmetric dimethyl arginine (ADMA), interleukin 18 (IL-18) and CD40 ligand (CD40lig) that were then appropriately logarithmically transformed.

Hypertensive subjects with OSA compared to the control group exhibited higher 24 hour systolic (140.5 ± 9.5 vs 137.7 ± 6.3 mmHg, $P = 0.019$) and diastolic (87.6 ± 6.9 vs 83.7 ± 7.1, $P < 0.001$) BP values. The metabolic profile and estimated glomerular filtration rate (GFR) were similar between the two groups. Left ventricular mass index (LVMI) and c-f PWV were also significantly increased in the group with OSA (109.6 ± 22.9

vs 101.9 ± 25.3 g/m^2, $P = 0.03$, 8.3 ± 1.2 vs 7.1 ± 1.3 m/s, $P < 0.001$ respectively). Moreover, levels of logADMA, logIL-18 and logCD40lig were all higher in hypertensives with OSA compared to the control group (−0.25 ± 0.09 vs −0.31 ± 0.08 μmol/L, 2.46 ± 0.12 vs 2.35 ± 0.16 pg/mL, 0.57 ± 0.38 vs 0.32 ± 0.43 μg/L respectively, $P < 0.001$ for all). In the entire population, logAHI was correlated to c-f PWV ($r = 0.35$, $P < 0.001$), logADMA (0.41, $P < 0.001$), logIL-18 ($r = 0.35$, $P < 0.001$) and logCD40lig ($r = 0.33$, $P < 0.001$). In a multivariate regression model, 24 hour diastolic BP ($b = 0.15$), c-f PWV ($b = 0.27$), logIL-18 ($b = 0.22$), logCD 40 ligand ($b = 0.21$) and logADMA ($b = 0.36$, $P < 0.05$ for all) were independent predictors of AHI. OSA severity is associated with diverse markers of vascular insult, thus potential multiple benefits of prompt therapy in patients with concomitant hypertension should be underlined.

Keywords: Sleep apnea; Inflammatory markers; Atherosclerosis; Hypertension

PO-41

MODULATION OF VASCULAR FUNCTION AND OXIDATIVE STRESS IN TYPE II DIABETES MELLITUS: EFFECTS OF ALPHA-LIPOIC ACID

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Background: Lipoic acid, a potent antioxidant, has been used as a dietary supplement to prevent and treat many diseases, including cardiovascular disorders and neurodegenerative disorders. We sought to determine the effects of alpha-lipoic acid on the metabolism and vascular condition in the Zucker Diabetic Fatty (ZDF) Type II diabetes rat model.

Methods: We treated ZDF rats with alpha-lipoic acid (ALA, 25 mg/kg/day, n = 7) or vehicle (Control, n = 7) for a 4-week period. Following treatment, we measured markers of oxidative stress and nitric oxide bioavailability. Vascular reactivity was evaluated in isolated aortic rings. As a determinant of endothelial function, serum asymmetric dimethyl arginine (ADMA) levels were performed at baseline and after the treatment period.

Results: Using the tail-cuff method, in comparison to Control, systolic blood pressure decreased by 11.6% and diastolic blood pressure decreased by 10.1% in the ALA group ($P < 0.05$). Treatment with alpha-lipoic acid increased low density lipoprotein oxidation lag time (CON: 53.4 ± 9.0 s; ALA: 90.9 ± 12.3 s, $P < 0.05$), suggesting increased resistance to oxidative stress. There was an increase in aortic mRNA levels of glutathione peroxidase and manganese superoxide dismutase (MnSOD) in the ALA group. In comparison to Control, ALA therapy reversed the contractile effect of phenylephrine in isolated aortic rings, suggesting enhancement of vascular function. ADMA levels were significantly lower in the ALA group (CON: 0.29 ± 0.07; ALA: 0.20 ± 0.06 μmol/L, $P < 0.05$).

Conclusions: Treatment with ALA has a favorable effect on vascular reactivity and endothelial function. Furthermore, the effects of ALA on oxidative stress suggest a favorable therapeutic approach in retarding the development of vascular complications observed in Type II diabetes mellitus.

Keywords: Oxidative stress; Diabetes mellitus; Vascular function; Endothelium

PO-42

ATHEROGENIC INDEX OF THE PLASMA AS MARKER OF OXIDATIVE STRESS AND ENDOTHELIAL DYSFUNCTION

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Background: Dobiasova y Frohlich introduced the Atherogenic Index of the Plasma(AIP). The clinical impact of AIP was seen in a study assessing the predictive value of various clinical and biochemical markers for angiographically defined CAD (aCAD).

Aims: To evaluate if AIP is related with adipokine (IL-6/Adiponectine) levels, circulating superoxide dismutase, ADMA and haematologic parameters (tPA/PAI-1)

Methods: N = 287, 23–93 years (58.86 ± 0.83), with high cardiovascular risk (HCVR) AIP = log [(TG)/(HDL-c)]. ADMA (μmol/L), SOD (U/mL) Il-6 (pg/mL), Adiponectine (μg/mL), tPA (pg/mL), PAI-1 (ng/mL) by EIA.
Statistical: Mean ± SEM. $\alpha = 0.05$. Mann–Whitney's U. Levene's test.

Results: Patients were distributed into terciles according to AIP values, comparing upper vs lower tercil (cut-off points: 0.052 and −0.166), we observed that AIP was related to the following adipokines: Il-6; $P = 0.020$; adiponectine: $P = 0.005$.
2. There were significant differences in circulating levels of SOD $P < 0.001$ and ADMA: $P = 0.030$.
3. *t*-PA) and PAI-1 acted the same: PAI-1 $P = 0.004$, *t*-PA $P = 0.012$.

Conclusions: In patients with moderate to HCVR, AIP is a good marker to show the behaviour of the more important adipokines and with an antagonic physiopathologic sense: high IL-6, low adiponectine.
2. Levels of SOD are decreased in subjects with high AIP, but in ADMA we observed the reverse, both alterations contributed to the vascular injury.
3. There is also more: we observed that in patients with a high AIP there is a procoagulant and hypofibrinolitic status that worsens all the previously described.

Keywords: Oxidative stress; Atherogenic index; Adipokines

PO-43

THE EFFECT OF ANGIOTENSIN CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN-II RECEPTOR ANTAGONISTS ON THE ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CHRONIC PULMONARY HEART WITH ARTERIAL HYPERTENSION

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Objective: To evaluate of the effectiveness of angiotensin converting enzyme inhibitor (ACE inhibitor) - enalapril (E), angiotensin-II receptor antagonist (ARA) - kandesartan (K) and their combination (E + K) in patients with chronic pulmonary heart (CPH) for the dynamics of endothelin-1 (ET-1) and vascular-endothelial growth factor (VEGF).

Material and methods: We have examined of 282 patients with CPH, including – 118 (41.8%) with arterial hypertension (AH) I degree and 76 (26,9%) with AH II degree. ACE inhibitor Enalapril (Enap, KRKA, Slovenia) and ARA kandesartan (kandesar, RANBAXY, India-USA-Canada) was administered by titration - from 2.5 to 10 mg/day and from 4 to 32 mg/day in accordance. By ELISA method we investigated of the blood concentration of ET-1 (pg/mL) using diagnostic kits of Peninsula Laboratories (USA) and VEGF (pg/mL) using a set of Cytimmune (USA) before and after 6 months of treatment.

Results: The analysis of the odds ratio of the dynamics of ET-1 and VEGF was showed that at CPL with decompensated heart failure of NYHA FC III the best clinical effect was with the use of the basis therapy (BT) + E + K (OR = 0.12; 95% CI 0,02–0,74; P = 0,014). In the case of CPH decompensation with development of CHF -FC III (NYHA) the absolute risk reduction (ARR) was achieved under the scheme BT + E + K (ARR - 0,35; 95% CI −0,02– −0,68). Combined use of enalapril and kandesartan at the background of basic therapy showed the decrease of ARR in patients with decompensated CPH and CHF -FC IV (NYHA) (ARR = −0,43; 95% CI −0,05 to −0,81). A similar dynamic appeared on the relative risk reduction (RRR).

Conclusions: Direction of ACE inhibitor enalapril and ARA kandesartan in patients with decompensated CPL and heart failure FC III - IV (NYHA) enhances the therapeutic effect and reduces the excessive production of ET-1 and VEGF.

Keywords: Angiotensin converting enzyme inhibitor; Angiotensin-II receptor antagonist; Chronic pulmonary heart; Endothelial function

PO-44

ASSOCIATIONS OF RENAL FLOW RESERVE WITH ENDOTHELIAL DYSFUNCTION IN ESSENTIAL HYPERTENSIVES

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Renal flow reserve (RFR) expresses the ability of the kidneys to augment their perfusion from baseline to a maximal value and is defined as the quotient of renal blood flow (RBF) at maximal hyperemia divided by RBF at baseline. Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase is a marker of endothelial dysfunction. In this study we examined the possible relationship between RFR with ADMA levels in essential hypertensive patients.

For this purpose, we studied 12 hypertensive patients (aged 58 years, five males, office BP 150/95 mmHg) with not significant stenoses in the renal arteries in the renal angiography. In order to assess RFR, a 0.014 in. Doppler flow wire (Flowire, Volcano) was introduced into the renal artery for the measurement of average peak velocity under baseline and maximal hyperemic conditions. RFR was calculated in response to bolus intrarenal administration of dopamine (50 μg/kg) as the ratio of hyperemic to basal average peak velocity of the distal vessel. Serum creatinine levels (sCr), glomerular filtration rate (eGFR according to MDRD formula) and ADMA were assessed from a morning blood sample.

Based on the mean value of RFR (1.73), hypertensives were classified into those with high (n = 6) and low RFR values (n = 6). Hypertensives with low RFR values compared to those with high values did not differ with respect to age, sex, office BP values and anthropometric characteristics. Although sCr and eGFR were similar between hypertensives with low and high RFR values (0.88 ± 0.11 vs 0.78 ± 0.11 mg/dL and 82 ± 9 vs 91 ± 15 mL/min/1.73 m^2, P = NS for both), patients with low RFR exhibited higher levels of ADMA compared to those without (0.62 ± 0.1 vs 0.42 ± 0.17 μmol/L, P = 0.042). In the entire study population RFR was negatively correlated with ADMA (r = −0.645, P = 0.032).

Hypertensives with normal renal arteries and impaired renal microcirculation, based on invasively assessed decreased RFR values, are characterized by endothelial dysfunction as reflected by higher ADMA levels.

Keywords: Endothelial function; Renal flow

PO-45

INCREASED ENDOTHELIN-1 VASOCONSTRICTOR TONE WITH PREHYPERTENSION

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Hypertension (BP ≥ 140/90 mmHg) is associated with enhanced endothelin (ET)-1-mediated vasoconstrictor tone. ET-1 system activity is thought to play an important mechanistic role in the development of elevated BP and cardiovascular disease (CVD). Prehypertension (BP 120–139/80–89 mmHg) is now recognized as an independent risk factor for CVD and atherothrombotic events. Currently, it is unknown whether ET-1-mediated vasoconstrictor tone is elevated with prehypertension. We determined: 1) if ET-1-mediated vasoconstrictor tone is elevated in prehypertensive adults; and, if so, 2) whether ET-1 vasoconstrictor tone contributes to impaired endothelium-dependent vasodilation in this population. Forearm blood flow (FBF; plethysmography) responses to selective ETA receptor blockade (BQ-123; 100 nmol/min; 60 min) were determined in 26 normotensive (NT; age: 55 ± 1 years; BP: 112/72 ± 1/1 mmHg) and 32 prehypertensive (PreHT; 56 ± 1 years; 128/79 ± 1/1 mmHg) adults. In a subset of subjects (n = 10 NT; n = 16 PreHT), FBF responses to non-selective ET-1 receptor blockade (BQ-123 + BQ-788) were determined. Additionally, endothelium-dependent vasodilation to acetylcholine (ACh; 8.0–32.0 μg/100 mL tissue/min) was measured in the presence and absence of selective ETA receptor blockade in 12 adults from each group. FBF responses to sodium nitroprusside (SNP; 1.0–4.0 μg/100 mL tissue/min) were also determined. BQ-123 elicited a significantly greater vasodilator response (~20%) in PreHT vs NT. The addition of BQ-788 to BQ-123 resulted in a further increase in FBF ($P < 0.05$) in PreHT but not NT. FBF responses to ACh, but not SNP, were markedly lower in PreHT (from 4.6 ± 0.3 to 12.6 ± 0.5 mL/100 mL tissue/min) than NT (from 4.9 ± 0.3 to 14.7 ± 0.8 mL/100 mL tissue/min). Co-infusion of BQ-123 did not affect ACh-induced vasodilation in NT, but resulted in an ~20% increase ($P < 0.05$) in PreHT; abolishing the group differences in endothelium-dependent vasodilation. In conclusion, ET-1-mediated vasoconstrictor tone is elevated with prehypertension, contributing to impaired endothelium-dependent vasodilation. ET-1 vasoconstriction may underlie the increased risk of developing hypertension and CVD in prehypertensive adults.

Keywords: Endothelial function; Prehypertension; Vascular function; Endothelin-1

Epidemiology/Special Populations

PO-46

MANAGEMENT OF HYPERTENSIVE PATIENTS IN FRANCE AS A FUNCTION OF GENDER AND CARDIOVASCULAR RISK: PARITE STUDY

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To compare ways of managing essential hypertension as a function of gender and cardiovascular risk (CVR)
Cross-sectional, multicentric study conducted in France with 654 cardiologists, each of whom included four consecutive, gender-paired patients with hypertension. Three thousand four hundred and forty patients included (53% M, 47% F); F were older and had a more sedentary lifestyle but smoked less, had less diabetes, were less obese and had less LVH ($P < 0.01$ for all).

ABP measurement	Females	Males	Total	*P*
Patients tested (n) %	(1621), 24.7	(1819), 24.1	(3440) 24.4	0.65
Patients controlled with diabetes or renal failure (n) %	(493), 7.1	(616), 8	(1109) 7.6	0.84
Primary endpoint: modification of anti-hypertensive treatment as a function of gender or CVR				
Low CVR (n), %	(81), 43.2	(20), 30	(101), 40.6	0.28
Medium CVR (n), %	(528), 54	(441), 52.8	(969), 53.5	0.72
High CVR (n), %	(1012), 56.2	(1358), 53	(2370), 54.4	0.12
Secondary endpoint: Modification of anti-hypertensive treatment as a function of gender in untested patients				
Treatment modification (n), %	(1,220), 68.9	(1,381), 66.3	(2,601), 67.6	0.16

The PARITE study did not show any differences between males and females in the management of essential hypertension, whatever the risk level.

Keywords: Hypertension management; Gender; Cardiovascular risk

PO-47

THE RELATIONSHIP OF RESISTANT HYPERTENSION AND TREATMENT OUTCOMES WITH TOTAL COMPLIANCE AND BRAIN NATRIURETIC PEPTIDE IN AN AFRICAN AMERICAN HYPERTENSIVE COHORT

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Resistant hypertension (RH) affects 8–30% of hypertensive patients. Blood pressure (BP) reflects the interaction between the vasculature, intravascular volume, and cardiac function. Accordingly, we investigated the relationship of RH with total arterial compliance (TACI) and a commonly available cardiac biomarker, brain natriuretic peptide (BNP).
The cohort (N = 156) were hypertensives with TACI and BNP values available prior to attainment of their JNC 7 goal BP who also had at least 1 follow-up visit. The period prevalence (presence of RH at any time point during observation) was determined according to the quartile of both TACI and BNP. The age-,sex-adjusted SBP, DBP and antihypertensive drug therapeutic intensity score (TIS) at the time of BP control was also determined.
The cohort was 85.3% African American and 67.3% female. Average baseline BP was 153.1/91.8 mm Hg while taking an average of 2.4 BP medications. Median follow-up was 7 months. The prevalence of RH at baseline was 14.7% while the period prevalence was 43.6%. The period prevalence of RH by ascending quartile of TACI was 66%, 36.8%, 40%, and 30.8% ($P = 0.008$); the corresponding prevalence across BNP quartiles was 37.8%, 48.8%, 45.0%, and 42.1% ($P = 0.8$). The average attained BP (mm Hg) and antihypertensive TIS score at the time of first BP control across these TACI quartiles was 122.3/73.4 (2.38), 120.7/72.5 (1.84), 122.4/75.3 (1.74), and 120.0/79.4 (1.52); ($P = 0.62$, $P = 0.03$, $P = 0.03$). Across BNP quartiles the values were 123.8/77.3 (1.57), 120.2/75.0 (2.06), 121.1/74.7 (1.90), and 120.4/72.8 (1.94) ($P = 0.13$, $P = 0.34$, $P = 0.69$).
Resistant HTN was more prevalent during follow-up than at baseline as more patients met RH diagnostic criteria after optimization of drug therapy. Low total arterial compliance was linked to higher prevalence of RH as well as to a greater level of antihypertensive therapeutic intensity at first attainment of JNC goal BP.

Keywords: Resistant hypertension; Total arterial compliance index; Brain natriuretic peptide; Antihypertensive therapeutic intensity score

PO-48

WHICH AMBULATORY BLOOD PRESSURE MONITORING PARAMETERS PREDICT MORTALITY IN ELDERLY SUBJECTS?

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It has not yet been determined which of the several ambulatory blood pressure (BP) monitoring parameters is associated with mortality in elderly hypertensive. Using Cox proportional hazards models we examined the ambulatory BP of 3859 patients aged less than 70 years (average 50 ± 14, 50% men), and 891 patients 70 years and older (average 76 ± 5 years, 48% men), who were followed

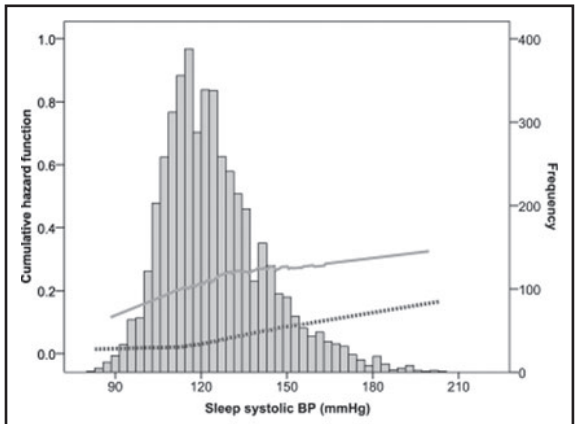

Figure: distribution of sleep SBP (histogram) and associated cumulative hazard adjusted for covariables (elderly subjects - solid line; yonger subjects - dotted line)

for all-cause mortality for up to 19 years. Patients in the older group were more likely to be treated for hypertension and diabetes, and had significantly higher manual and ambulatory systolic - and lower diastolic – BP levels. There was no difference in body mass index. Average sleep-related systolic BP dip was 12 ± 8% and 9 ± 9% in the younger and older groups respectively, $P < 0.0001$. Mortality was significantly higher among the elderly; 42 vs 7 deaths per 1000 patient-years (249 vs 275 events). Gender and obesity did not predict mortality. Diabetes did not predict mortality in the elderly; hazard ratio (HR) 1.39 [95% confidence interval (CI) 0.97–2.00] vs 2.82 (95% CI 2.08–3.83) ($P < 0.05$ for the interaction of diabetes with age group). After adjustment for age, gender, body mass index and treatment for diabetes and hypertension, neither manual-, 24-hour - or awake hypertension significantly predicted mortality in the elderly; HR were 0.78 (95% CI 0.59–1.04), 1.34 (95%CI 0.98–1.83) and 1.21 (95%CI 0.90–1.62), vs 1.69 (95%CI 1.22–2.34), 1.41 (95%CI 1.01–1.96) and 1.39 (95%CI 1.01–1.91) in the younger patients, respectively. However, sleep hypertension (figure) and non-dipping status (adjusted also for awake systolic BP) predicted mortality in both groups, HR 1.60 (95%CI 1.18–2.16) vs 1.76 (95%CI 1.28–2.42), and 1.47 (95%CI 1.15–1.88) vs 1.37 (95%CI 1.06–1.78) in elderly and younger patients, respectively. Thus in the elderly, conventional risk factors such as diabetes and clinic-, 24-hour -, and awake hypertension are not predictive of mortality while sleep hypertension and non-dipping pattern independently predict mortality.[figure1].

Keywords: Ambulatory arterial stifness index; Dipping; Elderly; Mortality

PO-49

BIRTH WEIGHT, STIMULUS RESPONSE AND HEMODYNAMIC VARIABILITY IMPLICATES ETHNIC CONTRASTS OF AUTONOMIC CONTROL OF HEART RATE AND BLOOD PRESSURE AND AN EFFECT ON CV DISEASE

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Marked race and sex differences for both heart rate and blood pressure (BP) have been reported beginning in childhood. Yet, pathophysiologic mechanisms mediating the changes of BP and heart rate (HR) are not fully understood.

BP is a highly variable physiologic trait which increases from childhood with body growth, while HR tends to decrease into adulthood. Studies have shown that variability of BP over 24 hour or over long-term periods are associated with an increase of cardiovascular (CV) and cerebrovascular events, even after adjusting for mean BP levels. Low birth weight is associated with greater variability and cardiac enlargement. In a Special BP Study of children (n = 273) stratified by low, mid and high levels of BP, it was observed that clinical and laboratory variables relating to BP and HR showed interesting racial contrasts with HR being slower and BP higher in blacks. Subjects stratified by BP levels were studied at rest, responses to orthostatic changes, hand grip and the cold pressure test. Stimulus from reactivity tests for BP was greater in blacks, suggesting a shift in autonomic control during stress. Of interest, the opposite occurred with HR being greater in white children.

With regards to long term BP observations blacks vs whites and males vs females showed greater variability. Further long term variability of systolic BP showed cardiac enlargement in blacks. These observations indicated a greater stimulus response and greater variability of BP in blacks and greater CV system damage in blacks.

Different mechanisms operating control of BP and HR are suggested. HR seems to be controlled more by the autonomic nervous system, while BP control may be even more complex through, not only autonomic balance, but by endothelial derived relaxing factor, status of the endothelium, RAA system, and structure of the vascular wall. Greater LVM index and other noninvasive studies have suggest CV damage from BP implicating endothelial integrity, NO reduction, RAA system changes and ANS response. The slower resting HR in black children, but faster HR and greater stimulus response of HR in whites, are consistent with more central control of HR, while various stimuli responses of BP in blacks suggest a more peripheral sympathetic control of BP.

Keywords: Stimulus response; Variability; Ethnic contrast; Blood pressure

PO-50

CHANGES IN LEVELS OF SERUM CHOLESTEROL AND DEVELOPMENT OF HYPERTENSION IN THE BRISIGHELLA HEART STUDY

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Rationale and objectives: Serum cholesterol (S-Chol) levels have been reported to affect blood pressure at young age and hypercholesterolemia might promote the development of hypertension (HTN) probably by activating tissue rennin-angiotensin system (RAS). The Aim of the present study was to assess the rate of development of stable HTN over a period of 8 years in a population of patients with normal/high-normal blood pressure with different control of S-Chol levels.

Methods: Nine hundred and thirty-two subjects enrolled in the Brisighella Heart Study with baseline BP values <140/90 mmHg and S-Chol levels from normal to elevated treated or not with lipid lowering drugs were subdivided in four different subgroups according to S-Chol changes over a period of 8 years (1996–2004). Group 1 and 2 include subjects whose S-Chol levels respectively remain or decreased within the normal range, while group 3 and 4 included subjects showing S-Chol levels persistently elevated ore increased above the normal range. The main measure of outcome was the incidence of stable HTN (BP > 140/90 mmHg and or treatment for HBP) over the period of follow-up.

Results: No major differences have been observed in the demographic and pressure profile between subjects in group 1–2 vs group 3–4. The 8-year incidence of HTN was 7.1% in group 1–2 and 13.8% in group 3–4 ($2P = 0.02$) and was significant for the main confounding risk factors. The difference between groups 1–2 and 3–4 was confirmed in male (8.2 vs 13.1%; $2P = 0.04$) and female (6.1. vs 14.5%; $2P = 006$) subjects while disappeared in the older population (<65 years = 5.7 vs 10.9%; $2P = 0.11$ and >65 years = 21.9 vs 25.9%; $2P = 0.081$). With each subpopulation of subjects (1/2 and 3/4) HTN rate was higher in subjects older and with higher baseline BP values but this does not affect the different control of S-Chol.

Conclusions: Serum cholesterol levels are related to the new onset of HTN and more aggressive strategy of lipid control could reduce the burden of CV risk beyond control of lipid profile.

Keywords: Cholesterol serum level; Hypertension

PO-51

ALCOHOL CONSUMPTION AND THE RISK OF HYPERTENSION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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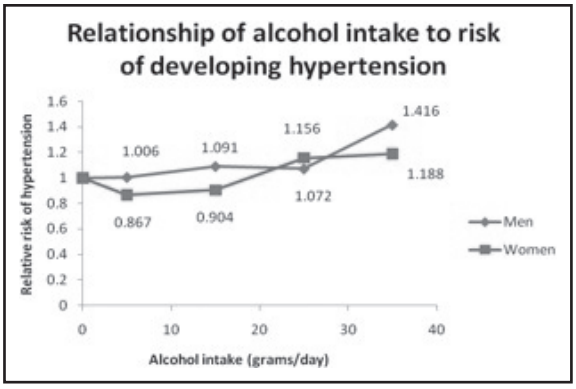
Background: Heavy alcohol intake increases the risk of hypertension, but the relationship between light-to-moderate alcohol consumption and incident hypertension remains controversial. We sought to analyze the dose-response relationship between average daily alcohol consumption and the risk of hypertension.

Methods: MEDLINE was searched for prospective control studies examining quantitative measurement of alcohol consumption and biological measurement of outcome. The primary endpoint was the risk of developing hypertension based on alcohol consumption. The level of alcohol consumption from each study was assigned to categorical groups based on the midpoint of their alcohol consumption classes to make possible the comparison of heterogeneous classification of alcohol intake. DerSimonian-Laird random effect model was utilized for the analysis, and publication bias was tested using funnel plot and testing Egger's publication bias.

Results: A total of 16 prospective studies with 158142 men and 31 4258 women were included in the analysis. Among men, a linear dose–response relationship between alcohol intake and risk of development of hypertension was noted. As compared to non-drinkers, men consuming < 10 g/day of alcohol had a relative risk (RR) of 1.006, those consuming 10–20 g/day had a RR of 1.091, and those consuming >30 g/day had a RR of 1.416. Among women, the meta-analysis indicated protective effects at <10 g/day (RR −0.867) and 10–20 g/day (RR – 0.904) of alcohol consumption, while the risk increased in women consuming >30 g/day (RR – 1.188).[figure1].

Conclusion: The risk for hypertension increases linearly with alcohol consumption in men. The relation between alcohol consumption and hypertension is J-shaped in women. The risk of hypertension significantly increases with consumption of more than 30 g/day in males and more than 20 g/day in females.



Keywords: Alcohol; Hypertension

PO-52

TRENDS IN ALBUMINURIA UNDER RAS SUPPRESSION AND RELATIONSHIP WITH CARDIOVASCULAR DISEASE

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Renin-angiotensin system (RAS) suppression is considered as the therapy of choice, together with a strict BP control, to prevent the development and to impede the progression of albuminuria.

We have reviewed the evolution of albuminuria in a group of 1433 patients (mean age 60.5 year; 50.3% male), arriving in our center unit. All had in common the existence of previous therapy with an ACEi or an ARB for a minimum of 2 years before arrival to our center.

When first seen 67.7% were normoalbuminuric, 11.9% exhibited high-normal values of albuminuria, 16.4% were microalbuminuric and 4% had macroalbuminuria. All of them were followed for 3 years during which RAS suppression was maintained. At the end of follow-up, only 54.9% were normoalbuminuric, 16.1% presented high-normal albuminuria, 21.6% were microalbuminuric and 7.4% macroalbuminuric ($P < 0.004$).

A total of 251 (17.5%) present previous cardiovascular disease at baseline and 69 (4.8%) develop new cardiovascular events during the follow-up. Among patients with normoalbuminuria or high-normal albuminuria at baseline, the progression to micro-macroalbuminuria was significantly higher in patients with previous cardiovascular disease than in those without it (17.2% vs 9.9%, $P = 0.003$). Also, this progression rate of albuminuria was higher in patients presenting new cardiovascular events during the follow-up than in those without it (18.9% vs 10.7%, $P = 0.057$). The multivariate regression analysis showed that factors related to the progression to micro-macroalbuminuria were serum glucose (odds ratio [OD] 1.014, 95% confidence interval [95%CI] 1.007–1.021, $P < 0.001$), serum creatinine (OR 2.293, 95%CI 1.366–3.850, $P = 0.002$), number of blood pressure lowering agents (OR 1.306, 95%CI 1.056–1.613, $P = 0.014$) and range of baseline albuminuria (normal or high normal)(OR 3.145, 95%CI 1.886–5.247, $P < 0.001$).

We conclude that albuminuria develops in the presence of chronic RAS suppression at adequate doses and progresses continuously. This progression is associated to the presence or development of cardiovascular disease. Long-term RAS suppression needs to be revisited in order to control this alteration.

Keywords: Renin-angiotensin system; Albuminuria; Cardiovascular disease; Arterial hypertension

PO-53

LARGE CHANGE IN THE OPINON ON ANTIHYPERTENSIVE DRUG TREATMENT AMONG GENERAL PRACTIONERS IN SWEDEN BETWEEN 2002 AND 2009

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Objective: To compare attitudes on drug treatment of hypertension among physicians in primary health care in Sweden between 2002 and 2009.

Design and Method: A population based sample (20–79 years) from the MONICA-study was used to randomly select hypertensive subjects with different risk profiles. The risk was classified in low, medium, high and very high risk according to the 1999 WHO/ISH Hypertension Guidelines risk stratification scheme. A total of 54 subjects were randomly drawn from the 4 different risk categories. Written case stories were constructed based on risk-factor levels for each selected subject. In 2002 155 doctors and 2009 218 doctors judged 12 cases each. The comparison was made on 1830 cases in (2002) and 2603 cases (2009) concerning willingness to initiate/give further drug treatment in subjects with uncontrolled hypertension (≥140/≥90 mm Hg).

Results: The willingness to initiate treatment both based on their own risk classification and WHO/ISH risk stratification scheme increased in all four categories (Table I). The largest increase occurred according to WHO/ISH risk estimate in the low risk group. According to the doctors own risk estimation the largest increase in willingness to treat occurred in the medium risk group. There were generally small differences in the willingness to give treatment depending on patient's sex except in the low risk group where men to less extent were given treatment.

Conclusion: The major finding is that the willingness to give drug treatment in uncontrolled hypertensive patients has increased substantially in all four risk categories. However, it still seems like some doctors hesitate to follow hypertension guidelines now in place since a decade.

Table I Physicians' willingness to initiate or give further blood pressure lowering drug treatment in the four risk group defined by 1999 WHO/ISH Hypertension Guidelines (a) or by physicians' own risk estimate (b)

(a)		
Risk group	2002	2009
(WHO/ISH)	Yes % (n)	Yes % (n)
Low	15.5 (17)	28.9 (110)
Medium	46.7 (149)	73.6 (289)
High	68.5 (222)	88.1 (285)
Very high	77.2 (416)	93.1 (609)
(b)		
Risk group	2002	2009
Own estimation	Yes % (n)	Yes % (n)
Low	27.6 (58)	29.2 (97)
Medium	53.1 (220)	72.3 (365)
High	78.3 (342)	91.5 (472)
Very high	85.6 (161)	97.4 (326)

Keywords: Attitude on cardiovascular risk; Doctors willingness to treat; Questionnaire.

PO-54

NOVEL METHOD FOR ASSESSING THE PREVALENCE OF HYPERTENSION AND CARDIOVASCULAR DISEASE RISK IN A COMMUNITY SCREENING PROGRAM IN A SOUTH EAST REGION OF US

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Purpose: To evaluate the prevalence of hypertension and cardiovascular disease(CVD) risk in Sarasota County, Florida utilizing early cardiovascular disease risk scoring system (ECVDRS), also known as Rasmussen Risk Score(RRS).

Methods: We evaluated 1891 consecutive asymptomatic subjects, majority self referred, who presented to our Center for CVD risk screening, age16–86; 874(46%) male and 1017 (54%) female. ECVDRS consists of 10 non-invasive tests: large and small artery stiffness(using Hypertension Diagnostics HDI DO-2020 device), blood pressure at rest and post exercise, carotid intima media thickness(measured by B-mode ultrasound according to a pre-specified protocol) and abdominal aorta ultrasound, retinal photography, Microalbuminura, ECG, LV ultrasound, and pro-BNP. Hypertension was defined as per JNC-7 criteria.

Results: Of the 1891 subjects screened, 751(40%) were identified as having hypertension by JNC-7 criteria. The subjects with HTN were divided into two groups: untreated 215(29%) and treated 536(71%). Of the treated subjects 180(34%) were not at BP goal. The majority of the untreated subjects(94%) were classified as intermediate to high risk for CVD by ECVDRS, but only 31% were classified as intermediate to high risk by FRS. In the treated group the intermediate and high risk subjects were 80% by ECVDRS, and only 14% by FRS.

Conclusions: 1. HTN appears to be very prevalent in this South East region of the US and in excess to what has been previously reported.
2. A significant number of subjects screened were not aware that they have HTN and therefore were not treated.
3. The majority of subjects with HTN were having early evidence for CVD as documented by ECVDRS.
4. FRS significantly underestimated the risk category in the majority of the hypertensive subjects regardless of their treatment status.
5. Based on our findings we urge community screenings using accurate tools for early CVD detection. This should be mandated and reimbursed for by those who care about our health as it is done with colonoscopy and mammography.
6. Hopefully such screening followed by appropriate medical management will avert or delay the onset of CV complications.

Keywords: Cardiovascular disease

PO-55

PRE-HYPERTENSION: IS IT A DISEASE?

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Objective/Purpose: To evaluate whether pre-hypertension is associated with structural vascular abnormalities utilizing the Early Cardiovascular Disease Risk Scoring System (ECVDRS), also known as Rasmussen Risk Score (RRS).

Methods: We evaluated a total of 1897 consecutive asymptomatic subjects who presented to our Center for Cardiovascular Disease (CVD) risk evaluation, aged 16–86, of whom 877 were male and 1020 were female. The majority of these subjects were self referred. ECVDRS consists of 10 non-invasive tests: large (C1) and small (C2) artery stiffness (using Hypertension Diagnostics HDI DO-2020 device), blood pressure at rest and post exercise, carotid intima media thickness(CIMT) (measured by B-mode ultrasound according to a pre-specified protocol) and abdominal aorta ultrasound, retinal photography, microalbuminuria, ECG, LV ultrasound, and proBNP. We defined pre-hypertension (pre-HTN) as per JNC-7 criteria.

Results: Of the subjects screened, 412(22%) were identified as having pre-HTN by JNC-7 criteria. At the time of the study, none of these subjects were taking an anti-hypertensive agent. The subjects were divided into two groups: males 203(49%) and

females 209(51%). The incidence of abnormal C2, CIMT and Hs-CRP in the male group was as follows: C2- 43(21%); CIMT - 89(44%) and Hs-CRP was normal in all subjects. In the female group 72 subjects (34%) had abnormal C2; 74(35%) abnormal CIMT and 2(0.01%) elevated Hs-CRP.

Conclusions: 1. Pre-hypertension is a disease as evidenced by vascular structural abnormalities including abnormal CIMT and C2.
2. The incidence of pre-hypertension appears to be equally distributed among males and females.
3. The biomarker for inflammation as measured by Hs-CRP was not a contributing factor.
4. Abnormal C2 appears to be more prevalent in the female individuals, while abnormal CIMT was more prevalent in the males.
Based on our data noninvasive screening for structural vascular abnormalities among pre-hypertensive individuals will help identify and stratify those at risk for CV morbid events. Those individuals may benefit from early treatment with medications such as ACE/ARBs which ultimately might reduce morbidity and mortality.

Keywords: Cardiovascular disease

PO-56

EXERCISE CAPACITY PREDICTS PROGRESSION FROM PRE-HYPERTENSION TO HYPERTENSION IN AFRICAN AMERICAN MEN

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Introduction: Predictors of the progression from pre-hypertension to hypertension (HTN) have not been adequately defined, especially in African-Americans. Since fitness is associated with cardiovascular health, we assessed the association between fitness levels and the rate of progression to HTN in pre-hypertensive African-American men.

Methods: We identified 1081pre-hypertensive African-American men (mean age: 54 ± 12) who underwent an exercise evaluation to rule out ischemia. All had a normal exercise response, were not receiving cardiac or antihypertensive medications and had resting blood pressure within the established pre-hypertension criteria. We established four fitness categories based on the age and MET level achieved. Individuals who achieved a peak MET level within the lowest 20th percentile of their respective age group (mean: 5.2 MET) comprised the Lowest-Fit category (n = 210). MET level between the 21st and 50th percentile (mean: 7.1 MET) comprised the Low-Fit category (n = 359). MET level between 51st and 80th percentile (mean: 8.6 MET) comprised the Moderate-Fit category (n = 308) and those with a MET level above the 80th percentile (mean: 10.1 MET), comprised the High-Fit category (n = 204).

Results: The overall rate of progression from pre-hypertension to HTN within the follow-up period of 8.2 ± 5.8 years was 33.3% and the yearly rate 4.1%. Cox proportional hazard analysis (adjusted for age, BMI, smoking, resting BP, and diabetes) revealed a 14% lower risk for developing HTN for every 1-MET increase in exercise capacity. The fitness-risk association was inverse and graded. When compared to the Highest-Fit category, the adjusted risk for developing HTN was 55% higher in the Moderate-Fit (hazard ratio = 1.55; CI: 1.1–2.2); 67% higher in the Low-Fit (hazard ratio = 1.67; CI: 1.1–2.3) and 82% higher (hazard ratio = 1.82; CI: 1.2–2.6) in the Lowest-Fit individuals.

Conclusions: Exercise capacity is inversely related to the risk for developing HTN. The risk was 14% lower for each 1-MET increase in exercise capacity. The relative risk for developing HTN in the two lowest fit categories was approximately 70% to 80% higher when compared to the High-Fit.

Keywords: Pre-hypertension; Hypertension; Exercise; African-Americans

PO-57

BIRACIAL (BLACK-WHITE) DIVERGENCE AND CORRELATES OF AUGMENTATION INDEX AMONG YOUNGER ADULTS: THE BOGALUSA HEART STUDY

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Historically, increased blood pressure has been related to a number of different Cardiovascular Outcomes. More recently, noninvasive measurements of central vascular parameters (particularly, *Augmentation Index –AI-*) have demonstrated to be more sensitive predictors of these outcomes in the general population. However, information is limited on the contrast and determinants of AI among racial groups (white/black); especially, in asymptomatic individuals.
The aim of this study was to assess racial/gender differences and predictors (determinants) of Augmentation Index in relatively young asymptomatic adults.
Noninvasive measurements of Augmentation Index (AI) where obtained through analysis of the radial arterial waveform by applanation tonometery (AT), in 705 participants (40.6% Male, 30.4% blacks) aged 29–50 years (mean of 43.3) from a biracial (black/white) semi-rural community. Association of conventional CV risk factors with AI, among race/sex groups, was also evaluated.
Significant race-gender differences were observed. After controlling for age & height, White females had significantly higher AI than white males (78.3 ± 13% vs 69.2 ± 13.7%, $P < 0.0001$); which was also observed in black females vs black males (87.8 ± 12.5% vs 72.8 ± 15.5%, $P < 0.0001$). Additionally, black females had significantly higher AI than white females (87.8 ± 12.5% vs 78.3 ± 13%, $P = 0.015$). Stepwise linear regression further revealed that African American ethnicity was consistently associated with increased AI values ($B = 3.26$; $P = 0.02$) and the impact of traditional CV risk factors among this race group, was also higher than in their white counterpart.
In this study of young asymptomatic adults, African American ethnicity conditioned higher levels of AI and accentuated the impact of traditional risk factors on this central vascular parameter, after adjustments for age & height. This observation may help to understand that vascular adaptation/modification to different risk factor exposure, differs within ethnic groups; with diverse incidence and intensity. Furthermore, this could also help for a better assessment of cardiovascular risk, by monitoring central vascular parameters changes in the population and paying special attention to the ethnic contrast.

Keywords: Augmentation index; Blood pressure; Racial contrast

PO-58

USE OF ELECTRONIC HEALTH RECORDS TO EVALUATE HYPERTENSION PHARMACOEPIDEMIOLOGY IN A PRIMARY CARE PRACTICE NETWORK

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Purpose: To demonstrate practical application of electronic health records (EHRs) as tools in hypertension (HTN) pharmacoepidemiology.

Methods: Retrospective study of a cohort followed longitudinally in the EHR of a 630,000 patient primary care practice network between 1998 and 2010. An extraction algorithm identified patients with new HTN diagnoses traceable in the EHR receiving pharmacotherapy for a 90-day minimum. Clinical data including blood pressure (BP), renal function, and exposure to antihypertensive drugs was obtained from the EHR. BP control (defined as both systolic <140 mmHg and diastolic <90 mmHg) associated with HTN pharmacotherapy was assessed.

Results: Nine hundred and two thirty patients were designated as having incident HTN diagnoses and being 'new users' of anti-HTN pharmacotherapy. Key baseline characteristics of the cohort were: age 51.8 ± 14.0 years; 54.9% female; 11% black, 6% Hispanic, 5% other, 78% white; mean onset from 1st documented EHR visit to HTN diagnosis 2.1 ± 2.4 years; creatinine 0.97 ± 0.31 mg/dL. Common initial medication regimens included monotherapy with ACE-I (35.6%), beta-blockers (12.3%), ARB (8.9%), calcium channel blockers (8.3%) and combinations of ACE-I/HCTZ (16.8), ARB/HCTZ (6.4%), and beta-blocker/HCTZ (2.4). 58.7% of patients in the cohort remained on their initial regimen without addition of another agent during the study period despite suboptimal control, reflected by approximately one-third of the BP measurements in this group being above 140/90 after more than 6 months of treatment. Increasing frequency of concurrent anti-HTN medications was inversely associated with blood pressure control (patients on three drugs had 39.9% of BPs uncontrolled, whereas those on ≥5 drugs had 51% of BPs uncontrolled). Outside of the cohort, occult HTN (≥2 BPs above 140/90 and absence of HTN diagnosis or anti-HTN medication history) was present in >46,000 patients (43% of all cases meeting BP criteria for HTN).

Conclusions: EHRs offer tremendous potential in advancing HTN pharmacoepidemiology and population health management. There continues to be a gap between HTN treatment guidelines and 'real-world' practice. EHRs can help target interventions to improve care at the patient and provider levels, and will be an important data source for HTN-related comparative effectiveness research.

Keywords: Hypertension pharmacoepidemiology; Electronic health records; Comparative effectiveness; Disease management

PO-59

CARDIOVASCULAR RISK FACTORS PREVALENCE IN GREEK HYPERTENSIVES STRATIFIED BY GENDER AND AGE

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Cardiovascular (CV) risk factors (RFs) and target organs damage (TOD) are common in hypertensive patients. The purpose of this study was to determine the frequency of clustering of RFs (dyslipidemia, smoking diabetes and obesity) and TOD (left ventricular hypertrophy - LVH, renal impairment) in Greek hypertensive patients stratified by gender and age.

This retrospective study comprised 21 280 adult patients with uncomplicated essential hypertension (11 309 males). Serum glucose, total cholesterol, HDL cholesterol, triglycerides, apolipoproteins A_1 and B were measured, left ventricular mass index (LVMI) and estimated gromerular filtration rate (eGFR) were calculated in all patients. In addition, total 10-years CV risk was estimated after calculation of the Framingham Risk Score (FRS) and the HeartScore (HS).

From 21 280 patients, only 10% had no concomitant RFs. More than half (53%) of the study cohort had one additional RF (49% dyslipidemia, 3% smoking, 1% diabetes). One out of 3 patients (33%) had two accessional RFs (26% dyslipidemia and smoking, 7% dyslipidemia and diabetes, 0.3% smoking and diabetes). The remaining 4% of patients studied had all four traditional risk factors. Furthermore, obesity was present in 30%, metabolic syndrome in 38%, low eGFR in 24% and LVH in 49% of all patients. According to FRS, mean CV risk was 35% for males and 24% for females while in high risk (>20%) were 69% of males and 51% of females. According to HS, mean risk for fatal CV events was 8% for males and 6% for females while in high risk (>5%) were 49% of males and 36% of females. A strong correlation was found between age and pulse pressure, eGFR, LVMI and CV risk in both genders. Ageing seems to increase the difference between males and females in total CV events but not in fatal CV events.

Hypertensive patients should be classified not only in relation to hypertension severity but also in terms of the total CV risk resulting from the coexistence of additional risk factors, organ damage and disease and decisions on treatment strategies should depend on the initial level of risk.

Keywords: Cardiovascular risk; Essential hypertension; Target organ damage

PO-60

ABO AND RHESUS BLOOD GROUPS AND CARDIOVASCULAR RISK IN ESSENTIAL HYPERTENSIVE PATIENTS

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Many studies have suggested an association between blood groups and various manifestations of heart disease. We have conducted the present study, in a large cohort of essential hypertensive patients, in order to assess any possible relations of different blood groups and the possible effect of the Rhesus system to total cardiovascular risk.

The study finally comprised 6533 essential hypertensive, non-diabetic patients who were subjected to physical examination, medical history, anthropometric measurements, repeated clinical BP measurement, blood sampling for routine laboratory examinations and 24-hour ABPM and echocardiographic study. Furthermore patients were divided according to the ABO and the Rhesus D antigene. Total 10-years cardiovascular risk was estimated after calculation of the Framingham Risk Score (FRS) and Heart Score (HS).

Patients were divided in two groups, Rhesus positive (n = 5462) and Rhesus negative (n = 1071). Furthermore, patients were

divided in eight subgroups according to ABO group and Rhesus blood group systems. Patients with B Rhesus negative blood group presented with the highest Framingham and Heart risk score while patients with AB Rhesus negative blood group with lowest. These differences remained significant even after adjustment for age and gender.
AB Rhesus negative phenotype offers protection against cardiovascular risk of essential hypertensive Greek patients with Rhesus blood type does not affect risk profile *per se*.

Keywords: Rhesus blood group; Arterial hypertension; Cardiovascular risk

PO-61

EFFICACY, SAFETY AND TOLERABILITY OF VALSARTAN/HYDROCHLOROTHIAZIDE SINGLE PILL COMBINATION IN ASIAN PATIENTS WITH ESSENTIAL HYPERTENSION: AN OBSERVATIONAL STUDY

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Previous studies have demonstrated that hypertensive patients need concomitant therapy with one or more drugs from different classes of anti-hypertensive agents to achieve their blood pressure control targets. We report the first multi-national, multi-center, 24-week follow-up observational study of valsartan/HCTZ single pill combination (SPC) in Asia to determine the efficacy, safety and tolerability in the treatment of essential hypertension. A total of 7567 patients who were diagnosed with Stage I or Stage II essential hypertension and took at least one dose of valsartan/HCTZ SPC were included into statistical analyses. Eligible patients received valsartan/HCTZ SPC 80/12.5 mg tablets orally once daily in the first 3 weeks. The subsequent dose was decided by the investigator according to the patient's clinical response. During the study, response rates and control rates increased continuously and reached 94.6% and 73.2%, respectively, at the end of the study. At week 24, mean systolic and diastolic blood pressure reductions were -25.4 mmHg and -14.9 mmHg, respectively. Using a four-point global assessment scale, more than 96.8% of the patients and physicians reported Good, Very Good, or Excellent for both their subjective efficacy and tolerability assessments. These results indicate that valsartan/HCTZ SPC is efficacious, well tolerated and devoid of any serious adverse effects in a real-world setting.

Keywords: Hypertension; Asian; Combination therapy; Efficacy

PO-62

TRENDS IN SERUM LIPIDS, HYPERTENSION, PHYSICIAN ADVICE AND COMPLIANCE AMONG REPRODUCTIVE-AGED WOMEN: UNITED STATES NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 1999–2008

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The objectives of this study were to examine trends in serum lipids, hypertension, obesity, and waist circumference (WC) among reproductive-aged women and how they related to physician advice and patient compliance with medication use for lipid abnormalities and hypertension. To accomplish this, we conducted trend analysis of these factors among 9818 reproductive-age women (16–49 year) using data obtained as a part of National Health and Nutrition Examination Survey (NHANES) between 1999 and 2008. To examine related hypotheses, we evaluated body weight, body mass index (BMI), WC, blood pressure (BP), serum lipids, self-reported hypercholesterolemia, self-reported hypertension, physician advice to reduce high cholesterol and hypertension, and patients' compliance with their advice. We also used prescription dataset to estimate the prevalence of prescribing actual lipid lowering medication. Multiple and logistic regression analyses were used to examine the linear trend over the 10-year period after adjusting for age, race/ethnicity and survey period. Overall, there was a significant linear upward trend for BMI ($P = 0.047$), WC ($P < 0.001$), and HDL cholesterol ($P < 0.001$) as well as an upward trend in the prevalence of obesity (BMI $\geq$ 30 kg/m^2) ($P = 0.050$) and abnormal WC (>88 cm) ($P = 0.013$). However, total cholesterol ($P < 0.001$), LDL cholesterol ($P < 0.001$), and triglyceride levels ($P = 0.037$) showed a significant downward trend over time. An upward trend was also observed with regard to percentage of women checked their blood cholesterol ($P < 0.001$), physician advice to take prescribed medicine for hypercholesterolemia ($P < 0.001$) and hypertension ($P = 0.001$), prescription of lipid-lowering agent ($P < 0.001$), and its patient compliance ($P < 0.001$). However, no significant changes in trend were observed for hypertension and self-reported use of antihypertensive drugs. Although both obesity and WC values rose significantly over the interval, serum lipid profiles improved which could be due to an increase in physician prescriptions for lipid-lowering medication and patient compliance with these medications.

Keywords: Trend analysis; Hypercholesterolemia; Hypertension; Lipid-lowering medication

PO-63

EXCESSIVE BLOOD PRESSURE ELEVATION DURING EXERCISE CORRELATES WITH LOW FITNESS AMONG NORMOTENSIVE FIREFIGHTERS

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Normotensives can excessively increase their blood pressure during exercise. The predictive value of such a response is still under debate. It can predict future hypertension, but in other studies it was related to survival benefit.
Firefighters represent a unique population because symptom limited maximal exercise stress testing simulates the physiology during fire suppression. The latter strenuous duty is associated with a markedly increased risk of cardiovascular mortality as compared to non-emergency duties.Firefighters with low cardiorespiratory fitness are at increased risk. The aim of our study was to examine the prevalence of peak exercise hypertension among normotensive firefighters, and to see wheter it correlates with low cardiorespiratory fitness.
We evaluated 995 career firefighters' maximal symptom-limited exercise tolerance time in seconds (in a fatigue-limited stress test). Hypertension was defined as resting readings $\geq$140/90 mmHg, or taking anti hypertensive medications. An exaggerated blood pressure response to exercise was defined as peak exercise blood pressure equal or above 220/90.

Exercise tolerance time was graded into quartiles, according to the time spent on the treadmill (in seconds). Quartiles represented low, moderate, high and very high fitness.
30.6% of the firefighters were hypertensive and excluded from further analysis. Of the remaining normotensives, 14% (93 out of 691) had an exaggerated blood pressure response to exercise. 31.1% of the "exaggerated BP" firefighters were in the low fitness group, compared to 18% in the normal responders ($P = 0.016$).
Only 13.5% of "exaggerated BP" group had high fitness (third quartile) compared to 30.6% in the normal responders ($P = 0.0024$).
Lower fitness is associated with a higher risk of an exaggerated blood pressure response. Firefighters with lower cardiovascular fitness may be prone to hyperactivate their sympathetic system, manifesting as extremely high blood pressure rise during exercise, and presumably during strenuous emergency duties.

Keywords: Peak exercise blood pressure; Stress test; Firefighters; Fitness

PO-64

SMOKING AND HYPERTENSION: DO THEY FOLLOW THE SAME TREND?

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Background: There is evidence, analyzing epidemiological surveys, that smoking habit is characterized periodically by a trend of increase, decrease and again increase in cigarette consumption. In addition, a close relationship exists between the effects of smoking and hypertension to determining cardiovascular risk.
Purpose of the study was to assess whether hypertension follows the same trend of smoking by a meta-analysis of studies on the subject.

Material and Method: The results obtained in the nine large-scale trials conducted from 1984 to 2009 as well as epidemiological surveys matched on the relationship of the trend between smoking and hypertension were examined. In addition, a meta-analysis of a previous meta-analysis examined in each of constituent articles was also conducted.

Results: Analyzed papers and number of investigated individuals derived from findings of Leone et al. (Min Cardioang, 1984), SHEP Study (JAMA, 1991), Verdecchia et al. (J Hypertens, 1995), HOT Study (Lancet, 1998), Primatesta et al. (Hypertension, 2001), Lewington et al. (Lancet, 2002), Vyssoulis et al (Am J Hypertens, 2002), Julius et al. (N Engl J Med, 2006), Masala et al. (J Hypertens, 2008). Periodic changes in smoking habit characterized by increase/decrease and again increase according to the power of anti-smoking campaigns were not accompanied by similar results in hypertensive subject. The latter took advantage merely of antihypertensive therapy and lifestyle and dietary changes.

Conclusions: Epidemiological surveys demonstrated undoubtedly that smoking habit followed periodically trends with increase, decrease and again increase in cigarette consumption related to the power of anti-smoking campaigns. The trend was not associated with a similar pattern of hypertension that showed rise or decrease depending merely on therapeutic treatment and dietary and lifestyle changes. However, synergistic association between smoking and hypertension in developing cardiovascular risk existed.

Keywords: Smoking trend; Hypertension; Antihypertensive therapy; Metaanalysis

PO-65

ARTERIAL HYPERTENSION AND LIVER CIRRHOSIS: THE EXPERIENCE OF A SINGLE LIVER UNIT

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Introduction: Liver cirrhosis is characterized by haemodynamic disfunctions, in particular hyperkinetic circulation and reduced effective volaemia. Therefore, cirrhotic patients are predominantly hypotensive or normotensive. However, arterial hypertension is present in some cirrhotic patients. Literature data demonstrated a prevalence of hypertension in cirrhotic population between 3% and 10%. The prevalence of arterial hypertension is 33% in males and 31% in females in general population in Italy [Italian Atlas of Cardiovascular Diseases, Ital. Heart J 2003]. Aim of this retrospective study was investigate the prevalence of arterial hypertension in cirrhotic patients referred to our Liver Unit.

Material and methods: We retrospectively analysed the charts of 420 patients with diagnosis of liver cirrhosis. Patients were 322 males and 98 females, with mean age of 63 ± 11 years. The etiology of cirrhosis was: viral hepatitis in 325 patients (69 hepatitis B-HBV-, 236 hepatitis C-HCV- and 12 co-infection HBV-HCV), alcohol in 76 patients, autoimmune diseases in seven patients, Wilson disease in two patients, criptogenetic in 18 patients. Mean follow-up was 39.2 months. We considered as hypertensive patients with arterial pressure >140/80 mmHg and patients treated with anti-hypertensive agents during overall follow-up.

Results: Diagnosis of arterial hypertension was confirmed in 38/420 (9%) patients with liver cirrhosis during a mean follow-up of 39.2 months. The history of 20 patients (20/420–4.7%) was characterized by initial diagnosis of arterial hypertension not confirmed during follow up or progressive normalization of arterial blood pressure during the follow-up, probably related to progression of liver disease.

Conclusion: Prevalence of arterial hypertension in cirrhosis is 9% in our study population. In our experience, this group of hypertensive cirrhotic patients presented persistently high arterial blood pressure and required anti-hypertensive treatment during a follow-up longer than 3 years.

Keywords: Hypertension; Cirrhosis

PO-66

BLOOD PRESSURE CONTROL AND AGE: THE EXPERIENCE OF A SINGLE CENTRE

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Aim of study: Aim of this study was to evaluate the control of hypertension in patients with different age and analyse the number of antihypertensive drugs in each class of patients.

Materials and methods: The clinical charts of 253 hypertensive patients were retrospectively reviewed; all patients were referred to our centre during a period of 16 years. They were men aged from 21 to 88 years old an all of them were treated with antihypertensive drugs (number of antihypertensive drugs taken from each patient: range 1–6). Patients were divided in groups according to age (<40, 40–49, 50–59, 60–69, 70–79, ≥80 years). The objective of antihypertensive treatment was considered arterial blood pressure ≤140/90 mmHg.

Results: Our data showed that arterial hypertension was respectively controlled (≤140/90 mmHg) in 39% of patients

<40 years, 37% of patients 40–49 years, 56% of patients 50–59 years, 51% of patients 60–69 years, 42% of patients 70–79 and 33% of patients ≥80 years. Not significant difference were observed between the use of more or less of 3 drugs in patients with or without optimal control of hypertension, except for patients over 80 years old. In this group, 50% of controlled patients was treated with ≤3 drugs and 50% with >3 drugs; 75% of uncontrolled patients was treated with ≤3 drugs and 25% with >3 drugs.

Conclusions: Patients aged from 50 to 59 had the best pressure control (56%) and over 59 this percentage decreases progressively with age. Despite the indication to take care about the number of drugs in older people, in our patients over 80 we need more than three drugs to obtain a satisfying pressure control.

Keywords: Hypertension; Pressure control

PO-67

THE EFFECT OF COFFEE ON BLOOD PRESSURE AND CARDIOVASCULAR DISEASE AMONG HYPERTENSIVE INDIVIDUALS: META-ANALYSIS

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Background: Most widely disseminated clinical guidelines on hypertension management do not comment on coffee consumption within the lifestyle recommendations.

Objectives: To summarize the evidence on the acute and longer-term effects of caffeine and coffee intake on blood pressure (BP), and on the association between habitual coffee consumption and risk of cardiovascular disease (CVD), among hypertensive individuals.

Design: Systematic review and meta-analysis.

Data sources: Publications written in English or Spanish identified in a Medline search up to 31 September 2010, and in references from published literature.

Review methods: Two independent investigators identified and extracted data from controlled trials on the effect of caffeine or coffee intake on BP change, and from cohort studies on the association between habitual coffee consumption and CVD.

Results: In 5 trials, the administration of 200—300 mg caffeine (the content of 1.5–2 cups of filtered coffee) produced a mean increase of 8.2 mm Hg (95% confidence interval [IC] 6.2–10 mm Hg) in systolic BP, and of 5.6 mm Hg (95% CI 4.2–6.9 mm Hg) in diastolic BP. The increase in BP was observed in the first hour after caffeine intake and lasted from at least 3 hour. Results held regardless of duration of caffeine abstinence before trial start, and of maintenance of antihypertensive medication. Study quality was heterogeneous because two trials were non-randomized, one did not mask caffeine administration, and two did not report whether BP measurement was based on two or more readings. In six trials on the longer-term effect (≥1 week) of coffee, there was no increase in BP when comparing caffeine vs placebo, coffee vs a caffeine-free diet, or coffee vs decaffeinated coffee. Moreover, coffee low in hydroxyhydroquinone and high in chlorogenic acids reduced BP. Quality of these trials was good overall. Lastly, five high-quality cohort studies provided no evidence of an association between habitual coffee consumption and higher risk of coronary disease or stroke.

Conclusions: Among hypertensive individuals, caffeine intake produces an acute increase in BP which lasts for at least 3 hours. However, present evidence does not support an association between longer-term coffee consumption and increased BP or increased risk of CVD among hypertensives.

Keywords: Systematic review; Meta-analysis; Coffee; Hypertension

PO-68

MECHANISMS UNDERLYING INCREASED AORTIC BP IN BLACK VS WHITE YOUNG ADULTS: THE ENIGMA STUDY

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The prevalence of hypertension is higher in black individuals compared with whites. However, the underlying hemodynamic mechanisms are not well understood.

Data from 306 Afro-Caribbean young adults (blacks, n = 306, mean age 22.5 years) and 400 randomly selected Caucasian controls (whites, n = 400, mean age 22.1 years) were available for the current analyses. All individuals were aged between 18–40 years and were free of cardiovascular disease and medication. Detailed demographic, biochemical and hemodynamic data including BP, cardiac output (CO), peripheral vascular resistance (PVR) and arterial stiffness were obtained in all individuals.

Compared with whites, blacks had an elevated BMI ($P = 0.001$) and an increased family history of hypertension ($P = 0.02$). Brachial systolic and diastolic BP and aortic systolic BP were also significantly higher in blacks ($P < 0.05$ for all comparisons). Regarding underlying hemodynamic mechanisms, CO and cardiac index were significantly lower in blacks than whites ($P < 0.001$ for both). However, PVR and PVR index were significantly elevated in blacks ($P < 0.001$ for both). This was accompanied by a significantly higher augmentation index (AIx, a measure of wave pressure wave reflections ($P < 0.001$), although aortic pulse wave velocity, a measure of large artery stiffness, was significantly lower in blacks ($P < 0.001$).

These data show that both brachial and central blood pressure are increased in black young adults compared with whites and that this may be related to abnormalities in the smaller resistance and pre-resistance vasculature, rather than the large elastic arteries.

Keywords: Central blood pressure; Racial differences; Hemodynamics; Arterial stiffness

PO-69

DIABETES TYPE 2 AND OTHER CARDIOVASCULAR RISK FACTORS IN AN ADULT MEDITERRANEAN POPULATION

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Purpose: Cassical epidemiological studies on diabetes (DM) underestimate the real problem because they only work with patients with known (K) DM. We have investgated the prevalences of DM, not known (NK) DM, other metabolic disorders and cardiovascular risk factors in a spaniard population.

Methods: On the basis of a two million community people and 64% older than 30 year-old, a stratified sampling of theese (1181) was obtained, 57%F and 43%M. After a detailed survey

and a medical examination, a fasting plasma glucose was determined and if it was betweenn 100–125 mg/dL a glucose tolerance test also was performed. According to the ADA criteria, subjects were assigned to normal (N), K-DM, NK-DM or impaired fasting glucose (IFG).

Results: The prevalence of K-DM was 10.7% (IC 95%:8.9–12.8); 12.5%M and 9.3%F, increasing in older people 2.4% (30–44 year), 6.0% (45–59 year), 16.6% (60–74 year), 21.5% (75 + year). Prevalence of NK-DM was 7.2% (IC 95%: 5.7–8.9); 9.1%M and 5.6%F. in our population K plus NK DM prevalence was 17.9% (IC 95%:15.5–20.6); 21.6%M and 15.0%F. Abnormal GTT were found in 5.6% and the prevalence of IFG were 22.3% (IC 95%:19.6–25.3); 26.2%M and 19.3%F. 65.2% subjects were Hypertensives (72.5%M; 57.2%F). Dislipidemia was found in 39.7% (40.7%F; 38.5%M). 43% had BMI > 30 (56%F; 30.3%M).

Conclusions: In our mediterranean population older than 30 year-old DM is more prevalent than most reported national or international clinical records. Only similar data were found in Cannary Islands, USA or WHO called high risk countries. DM increases with age and more in male. Near a half of diabetic patients do not know their own disease, more in younger people. More than 40% of people will develope glucose metabolic disease. There are many comorbidities in patients with DM which increase their cardiovascular risk.

Keywords: Diabetes; Epidemiology; Mediterranean population

PO-70

SERUM URIC ACID IS AN INDEPENDENT RISK FACTOR FOR CARDIOVASCULAR DISEASES MORTALITY IN HYPERTENSIVE PATIENTS

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The purpose of the study is to clarify the influences of serum uric acid (UA) on prognostic impact of cardiovascular disease and mortality in hypertensive patients, because there were several reports about cohort study with general population but not treated hypertensive patients.

Methods: The hospital-based cohort study employed 670 patients (male/female = 370/300; mean age = 62 ± 12 years old) with essential hypertension. The questionnaire included cause of death and the events of hypertensive complications, and the primary endpoint of this study was new onset of stroke or cardiovascular diseases (CVD; a new onset of angina pectoris, myocardial infarction, or heart failure). We evaluated baseline patients' characteristics including UA and assessed the ability to predict stroke and CVD. We also classified into four groups according to serum UA levels (more than 8.0 mg/dL = high (n = 27); 7.0–8.0 mg/dL = middle high (n = 60); 6.0–7.0 mg/dL = middle low (n = 143); <6.0 mg/dL = low (n = 440).

Results: During a mean follow-up period of 6.8 ± 3.0 years, 71 strokes, 59 CVD and 64 deaths were recorded. Kaplan–Meier analysis revealed that patients in the high UA group showed a higher frequency of stroke and CVD ($P = 0.0118$) and total mortality ($P = 0.0021$). A Cox proportional hazard model identified that serum UA level was predictive of CVD (relative risk = 1.24; $P = 0.0298$), stroke and CVD (relative risk = 1.18; $P = 0.0232$), stroke, CVD and death (relative risk = 1.16; $P = 0.0178$), but not stroke ($P = 0.3621$) and death ($P = 0.0685$) after adjustment for age, gender, diabetes mellitus, dyslipidemia, serum creatinine level and blood pressure.

Conclusions: The serum UA level might be an independent risk factor for stroke and CVD in patients with essential hypertension.

Keywords: Cohort study; Uric acid; Cardiovascular risk; Hypertensive patients

PO-71

BLOOD PRESSURE CONTROL AND ALL CAUSE MORTALITY IN OLD AND VERY OLD PATIENTS WITH HYPERTENSION

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The impact of blood pressure control on health outcomes, in elderly patients with hypertension has not been clearly defined. Among octogenarians, the HYVET study demonstrated improvement of cardiovascular complications when systolic blood pressure was reduced to 144 mmHg. Data with lower BPs in this population is not available. We examined mortality rates in 183 054 patients (age>70 years) with treated hypertension from 15 VA medical centers followed from 2000 to 2007. We divided patients in groups based on last achieved systolic blood systolic BP as follows: G1 > 150 (N = 34 309), G2: 140–149 (N = 28 028), G3: 130–139 (N = 45 908), G4: 120–129 (N = 33 143), G5:110–119(N = 20 748), G6:100–109 (N = 11 871), G7:<100 mmHg(N = 9047). During the follow up period blood pressure control improved from 45% in the year 2000 to 73% in the year 2007. During the 7 year follow up period a total of 45,039 patients died. Based on achieved systolic BP the lowest mortality rate (16.7%) was noted in G3 (SBP 130–139). Compared to G3, patients with higher achieved SBP experienced 40% (G1) and 17%(G2) higher mortality ($P < 0.001$). Patients with lower systolic BP (G4 to G7) also experienced higher mortality rates (22–408%, $P < 0.001$), thus forming a J shape curve. Similar results were noted when patients were grouped based on achieved diastolic BP. Optimal mortality was noted with achieved diastolic BP between 70 and 79 mmHg. Higher or lower diastolic BP were associated with higher all cause mortality. Mortality trends were similar in subgroups of patients age 70–79 and >80 years.

We conclude that (i) Optimal blood pressure control can be achieved in the old and very old populations and it is associated with improved mortality rates, (ii) In this population optimal systolic BP is 130–139 and optimal diastolic 70–79 mmHg, (iii)Reverse causality cannot be excluded for systolic <120 mmHg and diastolic<70 mmHg.

Keywords: Blood pressure control; Mortality; J shape curve; Elderly

PO-72

AMBULATORY BLOOD PRESSURE MONITORING PROFILE IN UNTREATED AFRICAN BLACKS AND CAUSASIANS UNTREATED HYPERTENSIVE PATIENTS MATCHED FOR AGE AND GENDER

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Few studies have evaluated 24 hour -ambulatory blood pressure (ABP) profile in black hypertensive patients (BHP) while living in

	Data							
	n BHP	n CHP	24 hour -BP (mm Hg) BHP	24 hour -BP (mm Hg) CHP	Dyslipidemia/ diabetes (%) BHP	Dyslipidemia/ diabetes (%) CHP	Nighttime BP fall (%) BHP	Nighttime BP fall (%) CHP
20–30 years	44	37	145/88	133/85*	25/3.5	33/6.6	7.8 ± 5.1	10.6 ± 7.3
31–40 years	143	105	147/94	134/86*	37/5.5	29/4.6	9.4 ± 6.2	10.8 ± 6.1*
41–50 years	199	190	147/95	138/87*	41/6.4	47/7.8	8.8 ± 7.1	11.4 ± 8.7*
51–60 years	118	148	150/93	140/86*	53/6.8	52/8.6	9.3 ± 7.5	11.5 ± 8.6*
61–70 years	31	113	144/85	139/82*	55/10	61/7.5	8.4 ± 7.1	11.4 ± 6.8*
>70 years	20	27	144/83	144/78	60/15	61/16	4.1 ± 7.3	8.4 ± 7.5*

*$P < 0.001$ vs BHPts.

Africa. The aim of that study was to compare ABP profile in never treated BHP of Mozambique (20–80 years) vs never treated Caucasians hypertensive patients (CHP) matched for age and gender. Only patients with 24 hour ABP ≥ 130/80 mm Hg were included. BHP were n = 555, 47 ± 12 years, 51% women, BMI = 28 ± 8 kg/m^2, 7% smokers; CHP were n = 620, 50 ± 13 years, 50% women, BMI = 27 ± 5 kg/m^2, 18% smokers ($P < 0.02$). vs CHP, BHP showed higher 24 hour, daytime and nighttime BP values and lower nighttime BP fall (in %) in almost all decades of age distribution (Table I, *$P < 0.001$ vs BHPts). Percentage of dydlipidemia and diabetes did not differ between groups. Heart rate 24-hour was significantly higher in BHP vs CHP only for 20–30 and 31–40 years. Differences between BHPts and CHPts were maintained significant when calculations were done separately for both men and women.

In conclusion our data suggest that untreated Africans BHP present systematically a higher ABP values and a lower nighttime BP fall than untreated CHP for all spectrum of age distribution. That may lead to a worse cardiovascular prognosis in BHP as compared with CHP.

Keywords: Ambulatory blood pressure monitoring; Black hypertension; Causacian hypertension; Untreated

PO-73

REGIONAL DIFFERENCES IN HYPERTENSIVE CARDIOVASCULAR REMODELING BETWEEN FISHING AND FARMING COMMUNITIES IN JAPAN

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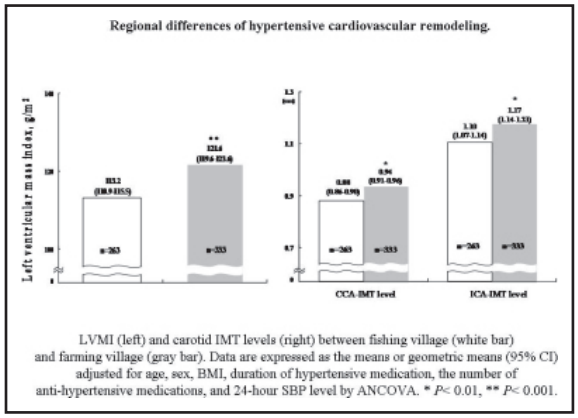
Background: Effects of dietary n-3 polyunsaturated fatty acids intake on the cardiovascular system have been reported, and thus we hypothesized that the prevalence of hypertensive cardiovascular remodeling would be lower in a fishing than a farming community.

Methods: We recruited 263 essential hypertensives from a fishing and 333 from a farming village; all subjects were ≥40 years (mean 73 years; 42%men). They were cross-sectionally examined for serum eicosapentaenoic and docosahexaenoic acid (EPA,DHA), asymmetric dimethylarginine(ADMA) levels, left ventricular mass index(LVMI), and common-carotid and internal-carotid artery(CCA,ICA) intima-media thickness(IMT).

Results: Compared to the patients in the farming village, those in the fishing village had higher serum EPA and DHA levels (63.3 vs 70.9 μg/mL, 137.2 vs 157.8 μg/mL) and lower ADMA levels (0.49 vs 0.47 nmol/mL; all $P < 0.05$). LVMI and both CCA-IMT and ICA-IMT levels were lower in the fishing than the farming village (113.2 vs 121.6 g/m^2, 0.88 vs 0.94 mm, 1.10 vs 1.17 mm:all $P < 0.01$) even after adjustment for age, sex, BMI, duration of hypertensive medication, number of anti-hypertensive medications, and 24-hour systolic BP level. The differences in LVMI and IMT levels between these communities also remained unchanged (all $P < 0.01$) after additional adjustment for the regional differences in EPA, DHA, and ADMA levels. A multivariable linear regression analysis showed that the difference in place of residence was independently associated with LVMI as well as with both CCA-IMT and ICA-IMT levels (all $P < 0.01$).

Conclusion: The prevalence of cardiovascular remodeling was significantly lower in patients in the fishing community than in those in the farming community. Further investigations are required to explain the mechanisms underlying this association.



Keywords: Regional difference; Cardiac hypertrophy; Intima-media thickness; n-3 Polyunsaturated fatty acids

PO-74

RELEVANCE OF ATRIAL FIBRILLATION IN A LARGE COHORT OF HYPERTENSIVE PATIENTS

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Hypertension is the most frequent cause of atrial fibrillation (AF) and the combination of hypertension and AF is associated with a particularly high stroke risk. The prevalence in the general population is 1%, increasing up to 9% in elderly.

Our study was intended to describe the prevalence of AF in a cohort of hypertensive patients followed at least 1 year in our hypertension unit from January-1975 to March-2010, and those factors related to the presence of AF from the beginning or their development during the follow-up.

We included 7924 hypertensive patients (mean age 60.7 ± 14.7 years, 53.7% female) with a mean follow-up period of 8.1 ± 6.5 years.

A total of 308 (3.9%) patients presented with AF: in 111 (1.4%) AF was present from the beginning and in 199 (2.5%) AF was developed during the follow-up.
Among patients aged below 40 years, 40–49, 50–59, 60–69 or older than 69 years, the prevalence of AF was 0.4%, 0.8%, 2.5%, 6.3% and 8.4%, respectively ($P < 0.001$). Among male these percentages were 0.7%, 1.2%, 2.8%, 6.9% and 6.3%, respectively, and 0.0%, 0.4%, 2.2%, 5.8% and 9.6% among female ($P < 0.001$ in both subgroups).
Patients with AF showed older age, more obesity and diabetes, higher systolic blood pressure values and higher number of blood pressure lowering-drugs than those without AF. They showed more left ventricular hypertrophy, increased urinary albumin excretion, reduced estimated glomerular filtration rate, and higher rate of previous cardiovascular disease.
Factors related with the presence of AF from the beginning were age (odds ratio [OD] 1.058, 95% confidence interval [95%CI] 1.034–1.082, $P < 0.001$), presence of left ventricular hypertrophy (OR 2.315, 95%CI 1.416–3.785, $P < 0.001$) and previous cardiovascular disease (OR 3.923, 95%CI 2.395–6.427, $P < 0.001$). Factors related with the development of AF during the follow-up were age (OD 1.074, 95%CI 1.054–1.094, $P < 0.001$), body mass index (OD 1.047, 95%CI 1.010–1.086, $P = 0.013$), presence of left ventricular hypertrophy (OR 2.077, 95%CI 1.392–3.099, $P < 0.001$) and previous cardiovascular disease (OR 2.574, 95%CI 1.752–3.784, $P < 0.001$).
We conclude that pre-existing and new-onset AF is a frequent finding in hypertensive patients, closely related with age and the presence of left ventricular hypertrophy and previous cardiovascular disease.

Keywords: Arterial hypertension; Atrial fibrillation; Left ventricular hypertrophy; Cardiovascular disease

PO-75

PERIODONTAL DISEASE SEVERITY AND ALBUMIN EXCRETION IN HYPERTENSIVE PATIENTS: A POSITIVE ASSOCIATION BEYOND SYSTEMIC INFLAMMATION

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We investigated the association of periodontitis severity to urinary albumin excretion in states of low and high systemic inflammation, in the setting of hypertension.
We studied 242 patients (mean age 51 ± 9 years) with untreated hypertension and periodontitis of varying severity. Subjects underwent ambulatory blood pressure monitoring, echocardiography and periodontal examination for evaluation of mean clinical loss of attachment (MCLA), gingival bleeding index (GI) and maximum probe depth (PD). From fasting blood samples we assessed metabolic profile and high-sensitivity C-reactive protein (hsCRP). The albumin to creatinine ratio was estimated from two morning nonconsecutive urine samples.
Based on the median values of hsCRP and ACR (1.67 mg/L and 10 mg/g respectively), our population was split into four groups: low ACR/low hsCRP (n = 65), low ACR/high hsCRP (n = 63), high ACR/low hsCRP (n = 51) and high ACR/high hsCRP (n = 63). Patients with high ACR had significantly higher 24-hour systolic blood pressure compared to those with low ACR, while the periodontal indexes differed among all groups. All periodontal indexes, hsCRP and the interaction of each periodontal index with hsCRP were independent predictors of ACR. Among periodontal indexes, MCLA was the strongest determinant of the high ACR/high hsCRP pattern.
In untreated hypertensive patients, severity of periodontal disease is associated with urinary albumin excretion in a dose-dependent manner, while systemic inflammation further enhances this association.

Keywords: Periodontitis; Albuminuria

PO-76

EFFICACY OF AMLODIPINE/OLMESARTAN MEDOXOMIL WITH OR WITHOUT HYDROCHLOROTHIAZIDE IN ELDERLY PATIENTS UNCONTROLLED BY MONOTHERAPY

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A prespecified subgroup analysis of elderly pts (aged ≥65 years) in a prospective, open-label titration study conducted in pts with hypertension uncontrolled on prior monotherapy is presented (SBP ≥ 140 mmHg [≥130 mmHg for pts with diabetes] and ≤180 mmHg and DBP ≤110 mmHg). Pts were switched, without washout, to amlodipine/olmesartan medoxomil (AML/OM) 5/20 mg and uptitrated every 4 weeks to AML/OM 5/40 mg, AML/OM 10/40 mg (to achieve a seated (Se) BP of <120/70 mmHg), AML/OM 10/40 + hydrochlorothiazide (HCTZ) 12.5 mg and AML/OM 10/40 + HCTZ 25 mg (to achieve a SeBP of <125/75 mmHg). The primary endpoint was the cumulative percentage of pts achieving SeSBP goal <140 mmHg (<130 mmHg if diabetes) by Week 12. Of the total cohort of 999 pts 228 were elderly. In the elderly subgroup mean age (±SD) was 70.2 ± 4.0 years, baseline BP was 155.1 ± 9.3/85.4 ± 8.9 mmHg, BMI was 28.7 ± 5.1 kg/m^2; 37.7% of pts had metabolic syndrome and 19.7% had type 2 diabetes. The primary endpoint was achieved by 76.7% of pts. Other goal achievement rates are shown in the Table.
Mean changes (±SE) from baseline in BP during the titration periods ranged from -14.5 ± 0.9/-7.8 ± 0.5 mmHg for AML/OM 5/20 mg to -28.5 ± 1.5/-12.4 ± 0.9 mmHg for AML/OM 10/40 + HCTZ 25 mg. By Week 20 a cumulative BP goal of <140/90 mmHg was achieved by 86.8% of pts. An ABPM study in a subset of patients showed that BP reductions were maintained throughout the 24-hour dosing interval. Treatment emergent adverse events (TEAEs) occurred in 137/228 (60.1%) and drug-related (DR) TEAEs in 71/228 (31.1%) pts. The majority of TEAEs were mild-to-moderate in severity. This well-tolerated, treat-to-goal treatment algorithm allowed a large proportion of elderly pts with previously uncontrolled hypertension to safely achieve BP control by Weeks 12 and 20 on an amlodipine/olmesartan-based regimen.

Table

Goal achievement	Cumulative[a] week 12 (%)	Noncumulative[b] week 12 (LOCF) (%)
SeSBP (<140 mmHg; <130 mmHg diabetes)	76.7[c]	65.2
SeBP (<140/90 mmHg; <130/80 mmHg diabetes)	75.8	64.3
Goal achievement	**Cumulative week 20 (%)**	**Noncumulative week 20 (LOCF) (%)**
SeBP (<140/90 mmHg; <130/80 mmHg diabetes)	86.8	74.5

[a]At any time point; [b]At visit; [c]Primary endpoint: LOCF: Last observation carried forward

Keywords: Elderly; Olmesartan medoxomil; Amlodipine; BP control.

PO-77

BLOOD PRESSURE THERAPY AND RISK OF CVD: FRAMINGHAM HEART STUDY EXPERIENCE

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Background: There is little information concerning blood pressure (BP) treatment and risk for incident cardiovascular disease (CVD) at different BP levels for adults in the community.

Setting: Prospective cohort design with up to 12 years of follow up.

Methods: Data were analyzed for the risk of cardiovascular disease (CVD) according to BP levels using the combined experience of the original and offspring cohorts of the Framingham Heart Study. This analytic strategy helps to investigate unexplained risks for CVD outcomes in observational studies.

Results: A total of 11 448 participants were categorized according to BP level and BP treatment status. There were 1466 first CVD events during follow up. Untreated optimal BP (<120/<80 mm Hg) was used as the referent, and all other BP categories were significantly associated with the development of a first CVD event in multivariable Cox regression analyses that were adjusted for sex, logarithm of age, logarithm of total cholesterol, logarithm of HDL cholesterol, current smoking, and diabetes status. Adults with higher BP levels experienced greater CVD risk, and at all BP levels there was greater risk for CVD events for persons on BP therapy.

Conclusion: Both BP level and BP treatment were significantly related to CVD risk after adjustment by traditional risk factors. These findings suggest that CVD risk associated with current blood pressure level can also be considered in the context of blood pressure therapy. Such results from prospective observational studies provide opportunities to further investigate residual and unexplained CVD risk and to improve our understanding of how risk factor information is used in CVD prediction algorithms.

Multivariable adjusted hazard ratio for bp level		
BP Level (mm Hg)	Not on BP therapy	On BP therapy
<120/<80	1.00 (referent)	1.61*
120 to 130/80 to 85	1.25*	2.50**
130 to 140/85 to 90	1.54**	2.21**
140 to 160/90 to 100	2.10**	2.75**
≥160/≥100	2.84**	3.22**
Number at risk	n = 9,818	n = 1,630
First CVD events	n = 1,088	n = 378

*$P < 0.05$, **$P < 0.001$ with adjustment for sex, smoking, diabetes and log of age, cholesterol, and HDL cholesterol.

Keywords: Epidemiology; Risk factors; Therapy

PO-78

ELDERLY, ATRIAL FIBRILLATION AND ARTERIAL HYPERTENSION MANAGEMENT

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Hypertension in elderly patients is well established cause of cardiovascular morbidity and mortality in our country. The aim of the study was to assess: (i) achieving goal values of blood pressure (BP) in elderly patients according to Guidelines ESC/ESH 2007; (ii) mean heart rate HR) (iii) therapeutic decisions in the management and (iv) number of antihypertensive drugs used for treatment in hypertensives and in hypertensive subgroup patients with atrial fibrillation AF in elderly hypertensive patients.

We studied 3991 consecutive patients living in community Stari Grad during their controlled examinations in out patient cardiology department during January-November 2010. There were 1074 (26.91%) hypertensive treated patients ≥65 years. They were divided into two groups: I group, men, n = 416, mean age 74.02 ± 6 years; and II group, women, n = 658, mean age 73.30 ± 6 years ($P = 0.25$). We analyzed percentage of achieving goal BP values, systolic and diastolic BP, heart rate values, drug chooses (monotherapy and polytherapy) and mean number drugs used for therapy for men and women including subgroups with AF.

Goal values (BP < 140/90 mmHg) were achieved in 397 (36.96%) hypertensive patients.

Mean office treated BP in men was 139/80 mm Hg and in women 142/81 mmHg. Mean HR values were in men 71.92 ± 10/min, and in women 71.13 ± 11/min ($P = 0.5$). Monotherapy was present in 96 (8.93%) and polytherapy in 978 (91.06%) patients. The most often used drugs were ACE inhibitors (57.91%). The fixed combination was used in 178 (16.57%). Mean number of drugs used in men was 2.60 ± 0.9 and in women was 2.61 ± 0.9 (P = ns) AF was present in 144 (13.40%) patients. Mean number of drugs used in AF subgroup in men (n = 70) was 2.67 ± 0.8 and in women (n = 74) was 2.68 ± 0.7 (P = ns).

Conclusion: Goal BP values were achieved in 36.96% elderly hypertensive patients. The mean HR was 71/ min. The most often used drugs were ACE inhibitors. Mean number of antihypertensive drugs used for treatment in elderly hypertensives including patients with AF was 2.6.

Keywords: Elderly; Fibrillation; Menagemet; Hypertension

Immune Mechanisms in Hypertension

PO-79

RENAL SPECIFIC SILENCING OF DOPAMINE D_2 RECEPTORS IN MICE INCREASES BLOOD PRESSURE AND PRO- INFLAMMATORY FACTORS

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Mice with disruption of the dopamine D_2 receptor ($D_2^{-/-}$) are hypertensive and present renal injury and inflammation. The renal expression of pro-inflammatory cytokines/chemokines such as TNFα, lymphotoxin A (Lta), macrophage chemoattractant protein 1 and 2 (MCP1/CCL2 and MCP-2/CCL8) is increased in $D_2^{-/-}$ mice. To avoid the confounding effects of systemic and '*in utero*' D_2R deletion we acutely silenced renal D_2Rs in mice. D_2R silencing siRNA (3 mg/day, D_2R siRNA) vehicle or non-silencing siRNA (3 mg/day, mock siRNA) as control were transfected via subcapsular infusion through an osmotic minipump for 7 days into the left kidney of uni-nephrectomized adult male mice (n = 6/ group). The expression of D_2R in the renal cortex was decreased in mice treated with D_2R siRNA compared with vehicle treated (59 ± 11 vs 100 ± 6.5, $P < 0.05$) and was unchanged in mock siRNA treated mice. Blood pressure determined under anesthesia before and after the infusion was increased in mice

treated with D_2R siRNA (98 ± 2 vs 118 ± 6 mmHg; $P < 0.05$) but not with vehicle (103 ± 1 vs 102 ± 2) or mock siRNA.
The mRNA expression of cytokines/chemokines was determined in renal cortex by qRT-PCR. Expression of TNFα (1.6 ± 0.6 vs 1 ± 0.04 fold, $P < 0.05$), Lta (1.8 ± 0.44 vs 1 ± 0.03 fold, $P < 0.05$) and MCP-2/CCL8 (2.1 ± 0.4 vs 1 ± 0.05 fold, $P < 0.02$) was increased in mice treated with D_2R siRNA compared to vehicle-treated mice. Infusion of mock siRNA did not produce any significant change. Our results show that acute downregulation of renal D_2Rs is associated with increased renal expression of pro-inflammatory factors. These results are similar to our findings in $D_2^{-/-}$ mice and suggest that deficient renal D_2R function may predispose to the development of inflammation and injury and hypertension. This is important since several D_2R polymorphisms that are associated with human essential hypertension and high blood pressure result in substantially decreased receptor expression and function.

Keywords: Inflammation; Kidney; Hypertension; Dopamine receptors

PO-80

MACROPHAGES REGULATE PRESSOR RESPONSES TO ENDOTHELIN-1

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Endothelin-1 (ET-1) is vasoconstrictive & proinflammatory with effects mediated by two receptors: endothelin-A (ETAR) & endothelin-B (ETBR). ETAR antagonism is beneficial in hypertension. We assessed the effects of ET-1 on human macrophage (Mϕ) activation & chemokinesis. We also assessed a role for Mϕ in ET-1 uptake & in responses to ET-1 in vivo using a murine model of selective Mϕ depletion.
Human monocytes were matured to Mϕ & expression of ETAR and ETBR protein assessed by immunofluoresence, Western blot, & RT-PCR. Mϕ were exposed to LPS/IFNγ or exogenous ET-1, & IL-6, IL-8, IL-10, & TNFα & ET-1 production, & MHC II & CD86/86 expression assessed. Mϕ migration towards ET-1 or MCP-1 was assessed using a transwell system. ET-1 removal by Mϕ was investigated by co-incubation with chloroquine (CQ, inhibitor of lysosomal acidification), protease inhibitors (PI), or ETAR (BQ123) & ETBR (BQ788) antagonists, respectively. We also assessed whether selective Mϕ depletion in CD11b-DTR transgenic mice altered pressor responses to ET-1.
Mϕ expressed ETAR & ETBR protein & mRNA. ET-1 did not activate Mϕ. Mϕ demonstrated chemokinesis in response to ET-1: no ET-1 vs ET-1 1 ng/mlvs MCP-1: 68 ± 8 vs 390 ± 103* vs 158 ± 12 (mean±SD, Mϕ/hpf, n = 4, *$P < 0.05$). Mϕ removed ET-1 from the media by 70 ± 14% (n = 12). Mϕ mediated ET-1 removal was inhibited by both PI (ET-1 1 ng/mL vs ET-1 1 ng/mL + PI: 65 ± 4 vs 34 ± 11%) and BQ788, but not BQ123 (ET-1 vs ET-1 + BQ788: 38 ± 10 vs 27 ± 6%* n = 4, *$P < 0.05$). ET-1 removal was not affected by CQ.
In vivo, ET-1 caused a pressor response in control & sham mice at the highest ET-1 dose. By contrast, DT treated CD11b-DTR mice were more sensitive to the pressor effect of ET-1 with a greater peak change in BP that lasted longer. Responses to angiotensin II were not altered.

Keywords: Endothelin; Macrophage; Blood pressure

PO-81

BMI INFLUENCES THE ASSOCIATION OF AN IL-6 POLYMORPHISM ON INCREASED INSULIN RESISTANCE IN A HYPERTENSIVE POPULATION

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Background: The -174G>C Interleukin-6 (IL6) gene polymorphism is associated with insulin resistance (IR) in both normotensives and diabetics, but has not been examined in hypertensives. BMI is known to modify this association, with obese CC carriers demonstrating greater IR. The underlying mechanism for this association is unknown; however an interaction between obesity, renin-angiotensin-aldosterone system (RAAS) activity, and inflammation may be involved.

Objective: 1. To examine the association between -174G>C and IR in hypertensives and determine if BMI modifies this association.
2. To explore whether the RAAS contributes to the underlying physiology of this association.

Methods: Caucasian hypertensives genotyped for the -174 G>C variant were studied from HyperPATH (N = 311). Phenotype studies were done after subjects consumed two diets: a high salt (200 mmol/day) and a low salt (10 mmol/day) for 7 days each. Subjects were admitted overnight after each diet and plasma glucose, insulin, IL6, plasma renin activity (PRA), and aldosterone was measured in the morning after an 8 hour fast. IR was characterized by HOMA-IR.

Results: Multivariate linear regression demonstrated that -174 G>C was significantly associated with increased HOMA-IR on both high ($P = 0.05$) and low salt ($P = 0.01$) diets adjusting for age, gender, BMI, IL6, and PRA levels. A significant interaction between-174G>C and BMI existed on both the high ($P = 0.007$) and low salt ($P = 0.003$) diets. CC carriers were more IR than G carriers in obese individuals. Further, obese CC carriers (BMI ≥ 30 kg/m^2) had significantly higher PRA ($P = 0.05$) and aldosterone levels ($P = 0.03$) than CC carriers with lower BMI (BMI<30 kg/m^2) on a low salt diet, and exhibited a similar, but non-significant, trend on high salt (PRA $P = 0.2$; aldosterone $P = 0.1$). A difference in PRA and aldosterone levels by BMI status did not exist in G carriers on either diet

Table I

ET-1 (nmol/kg)	Maximum ΔBP (mmHg)			Duration o pressor response (AUC)		
	Control	Sham	DT	Control	Sham	DT
0.01	-1 ± 4	+1 ± 1	+1 ± 4	+40 ± 69	+105 ± 148	+150 ± 131
0.1	-1 ± 3	+1 ± 1	+10 ± 5	+294 ± 509	+79 ± 34	+2665 ± 2108
1	+25 ± 5	+18 ± 3	+41 ± 15*†	+12287 ± 4234	+6059 ± 1	+49706 ± 30796§†

CD11b-DTR mice BP response to ET-1. Data are mean ± SD (n = 3, *$P < 0.01$, $P < 0.05$ vscontrol, $P < 0.01$ vs sham)†§Human Mϕ possess ETAR & ETBR. Mϕ are not classically activated by ET-1 but are chemotactic to ET-1. Mϕ remove ET-1 from their environment by ETB receptor mediated uptake and proteolytic degradation. In vivo, Mϕ depletion augments the pressor effects of ET-1. These data suggest a potential role for Mϕ in regulating the effects of ET-1 mediated hypertension.

suggesting that an overactive RAAS may be contributing to the BMI/CC carrier interaction effect on HOMA-IR.

Conclusion: The -174 G>C polymorphism is associated with IR in Caucasian hypertensives and BMI modifies this association. These findings are consistent with prior studies, extending the generalizability of the results to hypertension. Further, this study suggests an activated RAAS may be contributing to the polymorphism/BMI interaction.

Keywords: Interleukin-6; Renin angiotensin aldosterone system; Insulin resistance; Genetics

PO-82

CORRELATION BETWEEN ENDOTHELIAL DYSFUNCTION AND INFLAMMATORY MARKERS AT THE CHRONIC HEART FAILURE WITH ARTERIAL HYPERTENSION

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The chronic heart failure and arterial hypertension has a lot of biochemical manifestation. The ideas of our research work were: (i) to compare high sensitive C-reactive protein (hsCRP) and soluble receptors TNF alpha (sTNF-Rs) with coronary heart disease (CHD) and the chronic heart failure (CHF); in the control group (C group); (ii) to compare ultrasound markers of endothelium-dependent vasodilatation (EDV) and endothelium-independent vasodilatation (EIV) in hypertensive (HT) patients in both groups.

Patients and Methods: One hundred anf five hypertensive pts (mean age 63.4 years.), with CHD+CHF were investigated. In the NYHA classes I/ II/ III/ IV were 19/33/49/4 pts. The C group was represented by 20 healthy volunteers. Ultrasound assessment of flow mediated dilation (FMD) of brachial artery was used for the measurement of EDV and the response to isosorbide dinitrate (ISDN) for the measurement of EIV. sTNF-Rs and hsCRP were examined by the ELISA method.

Results: FMD was significant diminished in hypertensive pts. In 60th sec of reactive brachial artery hyperemia the luminal size has not reached the basal parameter (HT pts mean FMD: $94.9 \pm 11.0\%$, C group mean FMD: $109.1 \pm 7.3\%$, $P < 0.001$). EIV was significant reduced in HT pts comparing with C group (HT pts mean EIV: $105.7 \pm 19.6\%$, C group mean EIV: $118.0 \pm 10.2\%$, $P = 0.01$). In HT group significant elevated levels of hsCRP and sTNF-RI were found (HT pts mean hsCRP: 7.79 ± 4.12 mg/L, C group mean hsCRP: 3.83 ± 3.12 mg/L, $P < 0.01$; HT group mean sTNF-RI: 1148.4 ± 398.6 pg/mL, C group mean sTNF-RI: 632.2 ± 37.9 pg/mL, $P < 0.001$). No significant difference in sTNF-RII levels between the groups was found. Correlation between sTNF-RI and rest luminal size of brachial artery was observed ($r = 0.25$, $P = 0.05$). No other correlation between EDVa EIV and inflammatory markers was found.

Conclusion: Significant reduced endothelium-dependent and endothelium-independent vasodilation of brachial artery in HT pts was found. Significant elevated levels of hsCRP and sTNF-RI in these pts were measured, too. No significant correlation between ultrasound markers of endothelial dysfunction and inflammatory parameters was observed. Ultrasound assessment of endothelial dysfunction and inflammatory markers may give us an information concerning the severity and progression of disease.

Keywords: Endothelial dysfunction; C-reactive protein

Metabolic Syndrome (Diabetes/Glycemic Control; Dysglycemic Drugs; Insulin Resistance)

PO-83

SCREENING FOR DIABETES IN A DEVELOPING COUNTRY

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Background: Undiagnosed diabetes contributes significantly to the overall morbidity and mortality caused by the disease. Community-based screening is potentially a mechanism to identify patients with this condition, so as to identify pre-diabetes and institute prevention program.

Methods: Diabetes awareness campaign with free diabetes screening was conducted in a local community. During the screening program, 512 respondents between the ages of 18–80 years participated. Data obtained include FBS, BP measurements and demographic parameters. Data were analyzed using SPSS software version 11. A P value less than 0.05 was considered to be statistically significant.

Results: The mean age of the respondents was 44.9 ± 15.8 years. One thousand seven hundred and seventy-six respondents were females (62.3%) while 1076 (37.7%) were males. The mean body mass index was 26.6 ± 6.03. About halve of the respondents were found to be either overweight or obese. (Underweight = 3.4%, Normal = 42%, Overweight = 29.1%, Obesity = 25.5%). The FBS ranged 56–575 mg % with a mean of 109.3 ± 45.9 mg %. Twenty-two (4.3%) of the respondents were known diabetic patients compared with 490 respondents (95.7%) that were not known to be living with diabetes. Eight (36.4%) of the known persons living with diabetes had uncontrolled blood glucose, while 20 (4.1%) of the respondents that were not known to be living with diabetes had blood glucose level that indicated Impaired Fasting Glucose, IFG (Fasting blood sugar 110–126 mg%). Only 6 (1.2%) of the respondents had fasting blood glucose levels that indicated diabetes mellitus (FBS >126 mg%).

The mean systolic pressure was 128.8 + 18.6 mmHg with a range of 90–200 mmHg while the mean diastolic pressure was 82.1 + 12.4 mmHg and a range of 50–130 mmHg. Considering the diastolic pressure, more than one third (36.7%) of the respondents had either stage I or stage II hypertension (JNC 7 Classification). Only 96 (18.8%) of the respondents were known hypertensive patients.

Conclusion: Findings suggest that obesity is becoming a problem in Nigeria. IFG was detected among 4.3% while 1.2% had FBS that indicated diabetes. About 36.7% of the respondents had hypertension. Creating awareness on diabetes and instituting lifestyle modification measures to curb obesity, hypertension and diabetes are of paramount importance in our community.

Keywords: Screening; Diabetes; Obesity; Hypertension

PO-84

METABOLIC PROFILE AND FRAMINGHAM HEART SCORES AMONG HYPERTENSIVES IN TURKEY FROM 2003 TO 2007

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Background: Metabolic profile and cardiovascular risk assessment are crucial factors in management of hypertension and hypertension-related morbidity and mortality. The aim of the present study was to evaluate changes in metabolic profile and Framingham heart scores among hypertensive patients in Turkey from 2003 to 2007.

Methods: The data were extracted from a nationally representative sample who have participated in hypertension prevalence (n = 4910) and incidence (n = 3768) surveys conducted in the same cohort in 2003 and 2007, respectively. The number of hypertensives who were attained in both surveys was 1196. Blood pressure (BP) was measured by trained observers by means of a standard mercury sphygmomanometer. Fasting plasma glucose (FPG), triglyceridesi total and HDL cholesterol were obtained in patients and 10-year Framingham risk scores(FRS) were calculated both in 2003 and 2007 cohorts.

Results: Among hypertensive patients, 7.1% were known to be diabetics. In 4 years time, the percentage of FPG $\geq$ 126 mg/dL decreased from 46.4% to 35.7% in hypertensive patients who were aware of their diabetes. However, it was increased from 6.1% to 8.3% who had no diagnosis of diabetes. Triglyceride levels $\geq$150 mg/dL were increased in both known diabetics (from 53.3% to 56.7%) and the rest of the group(from 39.1% to 42.1%). Patients with low HDL cholesterol (<40 mg/dL for males and <50 mg/dL for females) were increased dramatically in both groups. In 4 years time patients with high or very high Framingham risk score ($\geq$20) were decreased from 30% to 26.6% in known diabetics but increased from 10.2% to 13.1%.

Conclusion: Hypertension is associated with a significant burden of metabolic risk factors and cardiovascular threat in Turkey. Although diabetes awareness might modify risk management strategies, the practitioner should be alert enough to capture the metabolic and cardiovascular risk factors for potential modifications.

Keywords: Hypertension; Diabetes; Cardiovascular risk; Epidemiology

PO-85

GENDER-INDEPENDENT ELEVATION OF FASTING GLUCOSE WITH THE PROGRESSIVE DECREASE IN SLEEP-TIME RELATIVE BLOOD PRESSURE DECLINE: THE HYGIA PROJECT

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Non-dipping has been associated with an increase in end-organ-damage and cardiovascular events. Non-dippers are more glucose intolerant than those with a normal dipper blood pressure (BP) profile. Moreover, elevated fasting glucose is significantly correlated with increased cardiovascular morbidity and mortality. We investigated the correlation between fasting glucose and the sleep-time relative BP decline in men and women participating in the Hygia Project, designed to evaluate prospectively cardiovascular risk by ambulatory BP monitoring (ABPM) in primary care centers of Northwest Spain. We studied 6120 subjects (3328 men/2792 women; 5370 hypertensive), 61.8 $\pm$ 13.5 years of age. Hypertension was defined as an awake BP mean $\geq$135/85 mmHg for systolic/diastolic BP, or an asleep BP mean $\geq$120/70 mmHg, or BP-lowering treatment. BP was measured by ABPM for 48 hour. Blood samples were obtained for each subject in the early morning after nocturnal fasting. Fasting glucose is characterized by a significant negative correlation with the sleep-time relative BP decline ($r = -0.114$; $P < 0.001$), and a positive correlation with the asleep BP mean ($r = 0.139$; $P < 0.001$). Correlations between glucose and awake BP mean, 24 hour BP mean, or clinic BP measurements were markedly lower. When subjects were divided according to the standard dipping classification, extreme-dippers and dippers showed the lowest average glucose (105 mg/dL). Glucose increased exponentially in the other groups (109 mg/dL in non-dippers, 118 mg/dL in risers; $P < 0.001$ between groups). Men showed an expected greater mean glucose than women (111 vs 105 mg/dL; $P < 0.001$), but the exponential increase in glucose with decrease in sleep-time relative BP decline was similar for both genders. Glucose is markedly increased in relation to the progressive loss in sleep-time BP regulation towards a non-dipper or even riser profile, independently of gender. Results suggest that a diminished sleep-time relative BP decline and elevated nighttime BP might be the most relevant ABPM characteristics for cardiovascular risk assessment.

Keywords: Glucose; Sleep-time blood pressure; Gender differences

PO-86

FIRST-LINE ALISKIREN/HCTZ LOWERS BP IN OLDER PATIENTS WITH STAGE 2 HYPERTENSION AND METABOLIC SYNDROME OR DIABETES

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Patients with stage 2 hypertension are at increased cardiovascular risk; the co-occurrence of metabolic syndrome (MetS) or type 2 diabetes mellitus (DM) raises this risk further. Current guidelines recommend initial treatment with two antihypertensive agents to achieve BP control. This was a subgroup analysis of patients with or without MetS (NCEP ATP III criteria) or DM from an 8-week study in older ($\geq$55 years) patients with stage 2 hypertension (mean sitting SBP [msSBP] 160–<200 mmHg). In all, 451 patients were randomized to aliskiren/hydrochlorothiazide (ALI/HCTZ) 150/12.5 mg or HCTZ 12.5 mg alone for 1 week, then double the doses for a further 7 weeks. Amlodipine 5 mg was added at weeks 4 or 6 if msSBP was $\geq$160 mmHg (data not shown). Treatment analyses were performed *post hoc*, by ANCOVA (BP changes) and logistic regression (BP control). At week 4 endpoint (primary), ALI/HCTZ provided significantly

larger msSBP reductions than HCTZ in patients with MetS/DM (Table), with an additional least-squares mean (LSM) reduction of 7.1 mmHg (95% CI: 2.9, 11.2; $P < 0.001$). ALI/HCTZ also provided similar msSBP reductions in patients without MetS/DM (additional LSM reduction 7.1 mmHg; 95% CI: 3.5, 10.6; $P < 0.001$). In both subgroups, BP control rates were significantly greater with ALI/HCTZ than HCTZ at week 4 endpoint ($P < 0.05$). Both treatments were generally well tolerated regardless of MetS/DM status. In conclusion, ALI/HCTZ provided significantly larger SBP reductions and improved BP control rates over HCTZ. Aliskiren/HCTZ may represent a highly effective treatment option for hypertension in older patients regardless of metabolic syndrome or diabetes status.

	With MetS/DM		Without MetS/DM	
	ALI/HCTZ 300/25 mg (n = 87)	HCTZ 25 mg (n = 104)	ALI/HCTZ 300/25 mg (n = 138)	HCTZ 25 mg (n = 118)
Mean baseline BP, mmHg	169.3/91.8	168.2/91.8	169.0/91.2	168.9/90.8
Change from baseline at week 4 endpoint, mmHg (least-squares mean ± SE)				
msSBP	-27.9 ± 1.6†	-20.8 ± 1.4	-30.8 ± 1.3†	-23.7 ± 1.4
msDBP	-8.7 ± 0.9*	-5.9 ± 0.8	-9.7 ± 0.7	-7.7 ± 0.8
BP control (<140/90 mmHg), %	47.1*	34.6	53.6†	32.2

*$P < 0.05$, †$P < 0.001$ vs HCTZ.

Keywords: Direct renin inhibitor; Metabolic syndrome; Diabetes

PO-87

EFFECTS OF TIME OF DAY OF HYPERTENSION TREATMENT ON THE AMBULATORY BLOOD PRESSURE PATTERN OF PATIENTS WITH DIABETES: THE HYGIA PROJECT

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Hypertensive patients with diabetes are at a greater risk for cardiovascular events than non-diabetic subjects. It has been reported that >89% of hypertensives ingest all their blood pressure (BP)-lowering medication in the morning. Moreover, non-dipping is associated, among other factors, with the absence of homogeneous 24 hour therapeutic coverage when subjects are treated with single morning doses. Accordingly, we investigated the impact of the time of day of hypertension treatment on the BP pattern of hypertensive patients with diabetes participating in the Hygia Project, designed to evaluate prospectively cardiovascular risk by ambulatory BP monitoring (ABPM) in primary care centers of Northwest Spain. We studied 1766 hypertensive patients with type 2 diabetes (1084 men/682 women), 66.5 ± 10.6 years of age. Among the subjects, 398 were untreated at the time of ABPM, 432 were treated with all BP-lowering medication ingested upon awakening, and the remaining subjects were ingesting ≥1 medication at bedtime. Hypertension was defined as an awake BP mean ≥125/75 mmHg for systolic/diastolic BP, or an asleep BP mean ≥110/60 mmHg, or BP-lowering treatment. BP was measured by ABPM for 48 hour. Among untreated patients, 62.8% were non-dipper (including 12.3% with a riser pattern). Among subjects ingesting all BP-lowering medication upon awakening, the prevalence of extreme-dipper, dipper, non-dipper and riser BP patterns were 4.2, 29.2, 49.3 and 17.4%, respectively ($P = 0.246$ for prevalence of non-dipper/riser pattern compared to untreated subjects). The prevalence of patients with sleep-time relative systolic BP decline <10% (non-dipping, including rising) was lowest among subjects ingesting all their prescribed medication at bedtime (53%; $P = 0.016$ compared to untreated subjects; $P < 0.001$ compared to patients treated upon awakening). In hypertensive patients with diabetes, treatment at bedtime is characterized by increased sleep-time BP control and a significantly lower prevalence of a non-dipper BP pattern. These two novel therapeutic targets have already been shown to significantly reduce cardiovascular morbidity and mortality.

Keywords: Chronotherapy; Diabetes; Ambulatory blood pressure

PO-88

OVERWEIGHT AND HIGH BLOOD PRESSURE AS THE CARDIOMETABOLIC RISK FACTORS MOST FREQUENTLY RELATED TO NONALCOHOLIC FATTY LIVER DISEASE

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Background: Non-alcoholic fatty liver disease (NFLD) is traditionally common in Gastroenterology and Internal Medicine offices but lately is also very frequent in Cardiovascular Risk polyclinics.

Methods: N = 333, aged 56.1 (14.2), 53% males, with moderate-high cardiovascular risk. Metabolic Syndrome (ATP III 2005). BMI (kg/m^2), waist(cm). Blood pressure (OMRON 705 CP). Glucose, triglycerides, cholesterol, HDL, LDL, (mg/dL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyltranspeptidase (GGT), alkaline phosphatase (ALP)]: HITACHI. Homocysteine (μmol/L): FPIA Abbott. Lp(a): (mg/dL). Nephelometric. sPLA2 (pg/mL). EIA. Cayman. ferritin (ng/mL): HPLC. HFE gene: ABI 7300 real-time PCR platform. Diagnosis of hepatic steatosis: abdominal echography or X-ray computed tomography. Statistical: Mean (SD). Normality by Kolmogorov–Smirnov test. Student-*t* test or Mann–Whitney-*U* test.

Results: 1. Twenty six percent (n = 88) of subjects presented NFLD, aged 54.6 (11.6), 22–82 years. 65% were males. 73% had hypertension, 56% with chronic hyperglycemia, 32% with T2DM and 57% with MSy.

2. According to BMI, 84% had overweight (43% with obesity). One out of two presented abdominal obesity.

3. History of hypercholesterolemia was observed in 56% and hypertriglyceridemia in 47% of NFLD patients.

4. Hyperferritinemia was present in 36%. Respect to genetic alterations related to hereditary hemochromatosis (HH): six patients were positive for H63D mutation, two homozygous and four heterozygous (carriers).

5. Seventy three percent (n = 64) of NFLD subjects showed abnormalities in the biochemical liver profile.

6. With regard to severity, patients with moderate or severe NFLD (27%) showed higher levels of: Ferritin: $P = 0.021$; AST: $P = 0.007$; $P = 0.003$; GGT: $P = 0.022$; and triglycerides: $P = 0.024$, and lower Lp(a): $P = 0.043$, than those with mild NFLD.

Conclusions: (i) Overweight and/or Hypertension are often associated with NFLD. (ii) One out of three subjects with NFLD had hyperferritinemia, that is the reason why a ferritin assay is mandatory in these patients. (iii) Surprisingly, history of hypercholesterolemia was more frequently related to NFLD than hypertriglyceridemia. Nevertheless, triglyceride, unlike LDL-c, were significantly bound to severity. (iv) Lower Lp(a) in moderate/severe NFLD deserves further research.

Keywords: Nonalcoholic fatty liver disease; High blood pressure; Overweight

PO-89

MYELOPEROXIDASE, LEPTIN AND RETINOL BINDING PROTEIN-4 AS BIOMARKERS OF OSTEOPENIA AND ATHEROSCLEROSIS, TWO SISTER-DISEASES

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Introduction: Increased evidence has been provided recently on the relationship between osteoporosis and cardiovascular disease. Both, leptin a RBP4 could contribute to insulin resistance and diabetes mellitus. Diabetes has been related to osteopenia but so far the relationship between leptin/RBP4 and osteopenia had not been reported. Finally, Myeloperoxidase activity, a new CV marker, has been inversely correlated with the bone formation indices, at least at experimental level.

Aims: To evaluate endothelial function in a population of moderate-high cardiovascular risk subjects with/without osteopenia.

Methods: N = 83, Aged 61.6 (11.0), 40–80 years; 55% males; 72% hypertensives; 72% hyperglycemics; 7% with CHD; 18% smokers. Population was divided into two groups according to *t*-score: Osteopenic ($t \leq$ -1) and Normal (t>-1). Densitometry: *t*-score and z-score were determined by quantitative ultrasonometry of the calcaneus (Achilles, GE Healthcare). Stiffness Index was calculated from broadband ultrasound attenuation (BUA) and speed of sound (SOS). Metabolic parameters: HITACHI. Leptin(ng/mL) and MPO(ng/mL) EIA BioVendor, Retinol-binding protein (RBP-4) (mg/L) EIA Immundiagnostik. Statistical: Mean (SD). Pearson's correlation coefficient. Normality by Kolmogorov–Smirnov test. Comparison between groups by Student-*t* test or Mann–Whitney-*U* test as appropriate.

Results1. Osteopenic subjects showed a lower stiffness index (SI) than those in the normal group: 72.9 (9.9) vs 104.6 (13.5), $P < 0.001$.
2. Leptin levels were increased in subjects with osteopenia: 23.2 (15.6) vs 14.4 (14.1), $P = 0.011$.
3. Higher MPO levels were observed in the osteopenic group: 82.3 (102.0) vs 40.3 (18.6), $P = 0.006$.
4. Both leptin ($r = -0.30$; $P = 0.006$) and MPO ($r = -0.25$; $P = 0.024$) were negatively correlated to SI.
5. RBP4: 29.7 (13.8) vs 24.7 (14.3), $P = 0.041$

Conclusions: Three new biomarkers related to Cardiometabolic disease are increased in osteopenic patients. Now we have new knowledge about the relationship between atherosclerosis and osteopenia. These findings could break new ground as many of the drugs exerting a cardiovascular protection may, at the same time, be beneficial for bone cell function.

Keywords: Osteoporosis; Leptin; Myeloperoxidase

PO-90

UNLIKE SEX, HDL-CHOLESTEROL, BODY MASS INDEX, HOMOCYSTEINE AND SMOKING, BLOOD PRESSURE IS NOT A DETERMINANT FACTOR OF PLASMA LEPTIN LEVELS

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Leptin is a adipokine related to patogenia of Metabolic Syndrome and reported as an independent cardiovascular risk factor in some epidemiological studies. Do we know the determinants factors of leptine?

Aims: To study the relationship between leptin and age, sex, classical CVR factors and emergent CVRF.

Methods: N = 144, 63.7 (12.6) years, 34–91 years, 52% males, 77% hypertensives, 71% hyperglycemics, 40% with T2DM, 10% with CHD and 20% smokers. Anthropometric: weight (kg), body mass index (BMI) (kg/m^2) and waist (cm). Glycemia, creatinin, HDL-cholesterol, LDL-cholesterol, total cholesterol and triglycerides, assessed by Hitachi autoanalyzer. Homocysteine (μmol/L): IMX, Abott Lp(a) (mg/dL): NLatex Lp(a) Reagent, Leptin (ng/mL) (ELISA BioVendor). Statistical analysis: Mean (SD). Pearson correlation coefficient. ANOVA. Multivariate linear regression: Backwards. Collinearity by Belsley. Model residuals.

Results: (1) Univariate analysis, after adjustment by sex and age, showed that leptin was associated with female sex ($P < 0.001$), age ($P = 0.007$), waist circumference ($P < 0.001$), BMI ($P < 0.001$), SBP ($P = 0.035$), CRP ($P = 0.042$) and physical inactivity ($P = 0.013$). (2) In multivariate analysis we observed that female sex ($\beta = 13.85$, $P < 0.001$), BMI ($\beta = 2.33$, $P < 0.001$), HDL-c ($\beta = 0.17$; $P < 0.028$) and Hcy ($\beta = 0.58$, $P < 0.038$) were independently and positively related to leptin plasma levels, after controlling by age, physical inactivity, type 2 diabetes, hypertensive status, systolic blood pressure, LDL-c., triglycerides, Lp(a) and CRP. (3) Smoking ($\beta = -5.35$; $P = 0.020$) had an inverse association with leptin levels. (4) The statistical model including these five variables accounted for a 55% of leptin variability (Adjusted R square = 0.547).

Conclusions: (1) Female sex is the main factor involved in plasma leptin levels. Body mass index and HDL-c also explain a part of total number. (2) Hcy, a non-traditional risk factor was independently and positively related to leptin plasma levels. (3) Neither hypertensive status nor blood pressure are determinant factors of plasma leptin levels. (4) Traditional and non-traditional CV risk factors – Now we know which ones relate to leptin and which don't.

Keywords: Leptin; Metabolic syndrome; Homocysteine

PO-91

SALT SENSITIVE TYPE 2 DIABETICS (T2D) HAVE GREATER METABOLIC IMPROVEMENTS ON A PALEOLITHIC-TYPE DIET COMPARED TO AN ADA DIET

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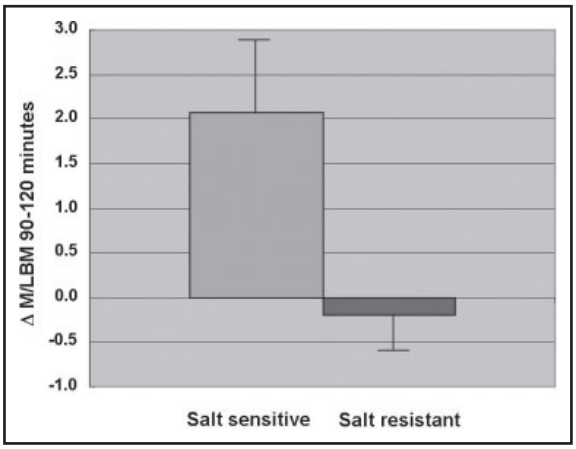
Background: Dietary salt can induce insulin resistance in both rats and men. As measured by glucose uptake in isolated soleus muscle, salt loading induced significant insulin resistance in the

Dahl-SS, but not Dahl-SR (salt resistant) rats. In normal weight Caucasian men placed in a 200 mmoL salt diet for 5 days, insulin resistance [mean insulin mediated glucose disposal (M values)] measured by euglycemic hyperinsulinemic clamp (EHC), increased ~15%.

Methods: T2D patients consuming their usual diets were randomized to a diet of lower salt content, either a 'Paleo'-diet (excludes dairy, legumes and grains) (n = 10) or a standard ADA diet (n = 8), for 2 weeks. All subjects had one EHC and flow mediated dilation study of the brachial artery (BAR, a measure of elasticity), and repeat fasting lipid, glucose and BP measures on the last 3 days of their usual and study diet. BPs were measured after 5 min sitting, in triplicate. Subjects were considered SS if BP decreased >5 mmHg with the study diets. All measures were averaged, results reported as mean ± SD.

Results: Both study diets improved glucose control and lipid values. The Paleo diet, however, induced greater improvements in fructosamine (P = 0.04) and total cholesterol (P = 0.08) compared to the ADA diet. BP did not fall with the ADA diet (=SR). BP fell with the Paleo-diet in seven subjects (=SS) and not in 3 (=SR) (MAP -8.5 ± 3.7 vs +5.6 ± 4.0 mmHg, respectively, $P < 0.001$). With the Paleo-diet, SS compared to SR subjects had bigger decreases in total cholesterol (Δ-39 ± 30 vs -12 ± 15 mg/dL), LDL-chol (Δ -25 ± 20 vs -1 ± 7 mg/dL), glucose (Δ -27 ± 30 mg/dL vs -19 ± 24 mg/dL) and fructosamine levels (Δ -33 ± 32 vs -20 ± 28 mmol/L). SS T2Ds also had greater improvement in insulin sensitivity (Δ M value +2.1 ± 2.8 vs −0.2 ± 0.6 (Figure). The SS T2Ds had a 19% improvement over baseline in BAR compared to 10% in the SR group (SR, 5.14 ± 0.31% to 5.7 ± 0.65%; SS, 5.17 ± 0.73% to 6.13 ± 1.16%).[figure1].

Conclusions: A Paleo-diet is superior to a standard ADA diet in improving metabolic abnormalities in T2D; and SS T2Ds particularly benefit from switching to the low salt Paleo-diet.



Keywords: Salt sensitivity; Insulin resistance; M values

PO-92

IMPACT OF GENDER IN CARDIOVASCULAR CONTROL IN HYPERTENSIVE PATIENTS WITH METABOLIC SYNDROME. OPENMET SURVEY

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We have studied the possible differences in the cardiovascular risk factors and their control according gender in a large number of hypertensive patients with metabolic syndrome (MS) attended in Primary Care centers in Spain.

Epidemiology, observational, cross-sectional multicenter Survey in Primary Care centers in Spain. The sample consisted in 3.655 patients (51.9% female),who were recruited consecutively during 1 month. MS was defined by NCEP-ATP III criteria.

Mean age was 60.4 ± 11.1 years, 51.9% female, BMI ≥ 30 kg/m^2 was 65.7% in male (M) and 58.9% in female (F); $P < 0.005$. Waist circumference 108.6 ± 11.6 cm (M) year 98.5 ± 12.8 cm (F) ($P < 0.0001$). Type 2 DM was presented in 54.4% of male and in 54.6% of women. Inadequate control ($HbA_1c > 7\%$) was found in 59.6% (M) and 56% (F). Most of them treated with oral antidiabetic drugs (93.4%), without significant difference between men and women. Monotherapy treatment with metformin was 44.6% (M) and 43,6% (F) (P = 0.54).

The percentage of BP control (<140/90 mmHg) in non-diabetic patients was only 25,3% (M) year 28.8% (F) (P = 0.12). Moreover, in diabetic patients, only 5% of male and 5,6% of female had a good BP control (>130/80 mmHg) (P = 0.6), in spite of most of them (98%) were under antihypertensive drugs (96% with RAS blockade).

We observed a very low percentage of patients with a good lipid control, only 15% of them had LDL-Chol <100 mg/dL without difference in gender; by contrast low HDL-Chol<40 mg/dL (M) o < 50 mg/dL (F) was presented in 43.4% (M) and 65.1% (F) ($P < 0.0001$); High levels of tryglicerides (≥150 mg/dL) was found in 22.1% (M) and 28.5% (F) ($P < 0.0001$). Nevertheless, we found a high proportion of patients with statin (85.7% (M) year 82,5% (F) (P = 0.008). Treatment with aspirin was reported in 34.6% (M) and 27.6 5 (F) (P = 0.0001).

In conclusions, the hypertensive patients with MS attended in primary care in Spain show a poor control of BP and cardiovascular risk factors. This OPENMET Study suggests that there are differences in the prevalence of some cardiovascular risk factors (obesity, lipid profile) and their treatment according gender, so this must be consider in order decreasing the cardiovascular risk in this population.

Keywords: Gender; Cardiovascular risk; Metabolic syndrome; Primary care

PO-93

MICROALBUMINURIA IN WOMEN WITH PRIOR GESTATIONAL DIABETES

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Women with prior gestational diabetes mellitus (pGDM) are at increased risk of developing type 2 diabetes and associated vasculopathy. The relationship between microalbuminuria, as a marker of cardiovascular risk, and glucose abnormalities was investigated in pGDM both at 3 months and 12 months after delivery.

We prospectively studied 198 women with pGDM. According to OGTT, we divided into two groups: pGDM with normal glucose tolerance post-partum (NG) (66.8%) and pGDM with abnormal glucose tolerance post-partum (AG) (33.2%). Insulin sensitivity was derived using HOMA. Metabolic syndrome (MS) was defined by ATP-III. We collected obstetric history, personal history of pGDM and personal and family history of cardiovascular risk factors.

The mean age was 33.45 ± 4.5 years.; 26,25% smoking, 15,6% history of dyslipemia, 30% had history of previous abortions. 62.34% of women had first-degree relatives with type 2 DM and 59.25% had family history of hypertension The prevalence of

MS was higher (32.3%) in AG group than in NG (14.7%); $P < 0.005$. In addition, AG group had higher values of BMI and WC vs NG group (28.86 ± 4.5 vs 22.70 ± 3.1 kg/m^2; $P < 0.005$ and 93.76 ± 6.1 vs 80.34 ± 4.6; $P < 0.05$, respectively). Fasting glucose and 2 hour -glucose levels were higher in AG group than NG (98.85 ± 7.7 vs 80.2 ± 5.6 mg/dL, $P < 0.005$ and 166.57 ± 23 vs 119.4 ± 20 mg/dL). Fasting insulin and HOMA values were significantly higher in AG than NG; $P < 0.005$. Microalbuminuria levels in AG group were greater (29.4 ± 13 mg/24 hour) vs NT (11.67 ± 4.7 mg/24 hour; $P < 0.05$). No differences in renal function. In addition, AG group presented a higher prevalence of family history of type 2 DM (68,7% vs 48%, $P < 0.01$).

In conclusion, women with pGDM have a high prevalence of abnormal glucose tolerance and MS. Microalbuminuria levels were in normal range although in AG group those values were higher than in NG group.. Thus women with pGDM and family history of type 2 DM may be especially suitable interventions aimed at preventing or reducing type 2 DM and probably cardiovascular events.

Keywords: Microalbuminuria; Glucose abnormality; Gestational diabetes; Insulin resistance

PO-94

ELEVATION OF BLOOD SUGER CHANGES GLOMERULAR AND TUBULAR FUNCTION IN NORMOTESIVE SUBJECTS

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Objective: Some patients present elevation of blood sugar(BS) before blood pressure(BP) increases. The aim of this study is to show that kidney takes part in the elevation of BP by making clear how renal function alters when BS elevates.

Design and Methods: Subjects were normotensive (<140/90) and never received treatment before or treatment in the least 3 months for hypertension(HT) and/or diabetes. Subjects with secondary HT and renal insufficiency (serum creatinine ≥1.0 mg/dL) were excluded. One hundred fifty-one normal BS subjects (NB) (HbA1c < 5.9% and fasting BS<110 mg/dL) and twenty-two high BS ones (HB) (HbA1c ≥ 6.5% or fasting BS≥ 126 mg/dL) were included. Urinary proteins and creatinine (Cr) were measured in a morning voiding urine sample. SDS-PAGE electrophoresis of urinary proteins was performed after the sample was concentrated with ultrafiltration. The protein content of the band by electrophoresis was calculated by the percent fraction of it times urinary total proteins/ creatinine ratio. e-GFR was calculated as previously reported.

Results: There were no significant age and BP difference between 57 year, 119/70 (NB) and 53, 123/72 (HB). Significant BMI difference existed between 23.2 kg/m^2 (NB) and 24.8 (HB) ($P < 0.05$). The urinary total proteins excretion corrected by creatinine was significantly different from 71.6 mg/gCr (NB) to 154.3 (HB) ($P < 0.001$). And e-GFRwas also significantly different from 84.9 mL/min/1.73 m^2 (NB) to 97.7 (HB) ($P < 0.001$). The content of 6 fractions in HB (192, 82, 64, 54, 35 and 27 kDa) was significantly increased. However, other 9 fractions (142, 100, 74, 48, 43, 23, 22, 11, and 9 kDa) were not significantly different in quantity.

Conclusions: Elevation of BS causes hyperfiltration of glomerus, and increase in glomerular and tubular protein excretion. These increase suggest impairment of glomerular and tubular function. Malfunction of nephron might take part of elevation of BP.

Keywords: Hyperglycemia; Proteinuria; Malfunction of nephron

PO-95

EFFECTS OF SIMVASTATIN AND ROSIGLITAZONE COMBINATION IN PATIENTS WITH THE METABOLIC SYNDROME (THE SIROCO STUDY)

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The purpose of this study was to test the hypothesis that a PPAR-gamma agonist will reduce inflammation and markers of oxidant stress in people with metabolic syndrome compared to statin use alone. The trial was randomized, double blind, and double dummy, placebo-controlled, comparing treatment with simvastatin plus placebo to combination treatment with simvastatin plus rosiglitazone. The primary endpoint of the trial was a > 30% reduction in the combined endpoint of malondialdehyde/urinary isoprostane concentration. Patients included in the trial were age 21–75 with LDL levels >130 mg/dL or >100 in patients with CHD and met criteria for metabolic syndrome by standard definition. Eighty-four percent (43/51) of the patients completed the study thus far, and presented. All patients received 3 weeks of simvastatin 40 mg/day prior to randomization and baseline data collection. Randomization was then to placebo or rosiglitazone at 4 mg once daily. All patients were followed for 6 months. Mean age was 61 ± 8, 49% were females and 44% were Black. The Table summarizes the demographics and primary endpoints.

We conclude that use of a PPAR gamma agonists significantly reduces oxidant stress and cardiovascular risk markers in people at risk for diabetes.

Demographic and Primary Outcomes

	Baseline	Six months
LDL (mg/dL)	103 ± 24	99 ± 29
SBP (mm Hg)	139 ± 13	137 ± 18
DBP (mm Hg)	81 ± 9	83 ± 9
Microalbuminuria (mg/day)	184 ± 67	92 ± 32*
Isoprostane (ng/mL)	1.84 ± 1.6	0.72 ± 0.2*
Malondialdehyde (pmol/mg)	10.1 ± 1.84	7.1 ± 0.84**

*$P = 0.03$;**$P < 0.001$

Keywords: Diabetes; Oxidant stress; Microalbuminuria; Metabolic syndrome

PO-96

PULSE WAVE ANALYSIS IN TYPE 2 DIABETIC HYPERTENSIVE PATIENTS

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Background: Cardiovascular risk is more severe in hypercholesterolemic hypertensive subjects with (Diab+) than without

(NoDiab) diabetes mellitus and is expected to differ in terms of pulsatile arterial hemodynamics including pulse wave velocity (PWV), wave reflections (WR), pulse pressure amplification (PPA).

Material and methods: Hypertensive subjects are divided into two groups for the same age, sex, heart rate, and mean blood pressure (MBP >105 mmHg) 216 NoDiab and 122 Diab+ subjects with 51 under and 71 without insulin treatment. Pulse wave analysis was performed in all patients.

Results: PWV was markedly higher ($P < 0.001$) in Diab+ than NoDiab subjects with, in the former group, a significantly higher beta index relating PWV to pulse pressure. WR was significantly lower in Diab+ than NoDiab subjects. Under insulin treatment, PWV, but not WR and PPA, was increased significantly.

Conclusion: Diabetic subjects have more severe pulsatile arterial hemodynamics than non-diabetic subjects for the same MAP, i.e. with high PWV, low WR and unchanged PPA, resulting in a more disturbed cardiac function. Insulin treatment and PWV, but not WR and PPA, are positively associated.

Keywords: Hypertension; Type 2 diabetes and insulin; Arterial stiffness; Wave reflections

PO-97

CIRCADIAN BLOOD PRESSURE PATTERN AND PREVALENCE OF NOCTURNAL HYPERTENSION IN SUBJECTS WITH AND WITHOUT TYPE 2 DIABETES: THE HYGIA PROJECT

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Non-dipping is associated with elevated risk of target organ damage, particularly to the heart, brain and kidney. Some studies have reported a relatively large prevalence of non-dipping in patients with type 2 diabetes mellitus (DM), although in most cases without proper comparison with subjects without DM. Accordingly, we studied the impact of DM on the circadian blood pressure (BP) pattern in subjects participating in the Hygia Project, designed to evaluate prospectively cardiovascular risk by ambulatory BP monitoring (ABPM) in primary care centers of Northwest Spain. We studied 7087 subjects (3848 men/3239 women; 1804 with DM), 61.4 ± 13.8 years of age. Among the subjects, 6216 were hypertensive, and among these 1766 had DM. Hypertension was defined as an awake BP mean ≥135/85 mm Hg for systolic/diastolic BP, or an asleep BP mean ≥120/70 mm Hg, or BP-lowering treatment. These thresholds were reduced by 10 mmHg in DM. BP was measured by ABPM for 48 hour. Among subjects without DM, the prevalence of extreme-dipper, dipper, non-dipper and riser BP patterns were 4.3, 44.5, 43.1 and 8.1%, respectively. The prevalence of non-dipping and rising were greater among patients with DM (46.7 and 17.1%, respectively; $P < 0.001$). The prevalence of rising was highest among treated hypertensive patients with DM (18.9%). Elevated sleep-time BP was a major factor for the diagnosis of hypertension in DM; thus, 95.9% of the uncontrolled hypertensive patients with DM had nocturnal hypertension. This cross-sectional study documents the high prevalence of an altered circadian BP pattern in DM. Most important, the prevalence of a high-risk riser BP pattern is more than double in DM than in subjects with DM, either they have hypertension or not. The elevated sleep-time BP mean in DM leads to a very high prevalence of nocturnal hypertension and, thus, to misdiagnosis of hypertension when identification of the condition is based on clinic or even awake BP determination. These results support ABPM as a clinical requirement for proper cardiovascular risk stratification among patients with DM.

Keywords: Diabetes; Nocturnal hypertension; Ambulatory blood pressure

PO-98

INFLUENCE OF SLEEP-TIME BLOOD PRESSURE FOR THE PROPER IDENTIFICATION OF ISOLATED OFFICE AND MASKED HYPERTENSION AMONG PATIENTS WITH TYPE 2 DIABETES: THE HYGIA PROJECT

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Target organ damage and cardiovascular (CVD) risk are more closely associated with ambulatory (ABPM) than with clinic blood pressure (BP). Accordingly, masked hypertension (HTN) has been associated with higher CVD risk than normotension and isolated-office (white-coat) HTN. Independent studies have also found that the sleep-time BP mean is a better predictor of CVD risk than the awake or 24 hour BP means. However, isolated office and masked HTN are frequently defined by comparing clinic with awake BP, disregarding the value of nighttime BP. We evaluated the impact of using sleep-time as well as awake BP for the diagnosis of isolated-office and masked HTN in patients with diabetes participating in the Hygia Project, designed to evaluate CVD risk by ABPM in primary care centers of Northwest Spain. We studied 1804 patients with type 2 diabetes (1097 men/707 women), 66.4 ± 10.7 years of age. Among the subjects, 1766 had HTN, defined as an awake BP mean ≥125/75 mmHg for systolic/diastolic BP, or an asleep BP mean ≥110/60 mmHg, or BP-lowering treatment. BP was measured by ABPM for 48 hour. Among uncontrolled hypertensive patients with DM, 95.9% had nocturnal HTN. Using both awake and sleep-time BP thresholds in comparison with clinic BP (130/80 mmHg), the prevalence of normal BP, isolated-office, masked and sustained HTN were 3.7, 5.3, 13.1 and 77.9%, respectively. Using only awake BP in comparison with clinic BP, the prevalence of the four classes were 8.3, 15.3, 8.5 and 67.9%, respectively ($P < 0.001$ compared to the previous classification). The prevalence obtained using only asleep BP for classification was 4.3, 8.5, 12.5 and 74.7%, respectively. Elevated sleep-time BP mean is a major factor for the proper diagnosis of HTN in patients with DM. The use of only awake BP mean in comparison with clinic BP values for the identification of isolated-office and masked HTN is totally misleading and provides false estimations of these two conditions, markedly different in terms of CVD risk. In DM, both awake and asleep BP derived from ABPM should be used to diagnose HTN and to properly stratify CVD risk.

Keywords: Sleep-time blood pressure; Masked hypertension; Diabetes; Isolated office hypertension

PO-99

SUBOPTIMAL CONTROL OF ARTERIAL HYPERTENSION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Aim: Treating arterial hypertension (AH) in patients with type 2 diabetes mellitus (DM2) is essential for preventing cardiovascular disease. Therefore, strict control of arterial hypertension should be achieved. Aim of the present study was to investigate whether DM2 patients are adequately treated for their hypertension.

Subjects/Methods: Seventy-five (20 males) DM2 patients with personal history of AH were recruited from the outpatient Clinic of Metabolic Diseases Unit. Arterial hypertension was measured in sitting position after 5 min rest, three times and a mean value was calculated. JNC7 recommendations were used for estimating adequate AH control. Anthropometric and biochemical parameters were estimated.

Results: The mean age of the sample was 61 ± 10 and body mass index was 36.3 ± 7 kg/m^2. No drug treatment was applied to 10 (13.3%) patients. In 67 patients (89.3%) AH was not adequately controlled. The average number of drugs used per patient was 2.3 ± 1. Angiotensin II converting enzyme inhibitor (ACEI) was used in 21 patients (28%) and angiotensin receptor blocker (ARB) was used in 33 patients (44%). In 35 patients that needed a second drug, a diuretic was used. In 10 patients (13.3%) a different anti-hypertensive agent was used.

Conclusion: Even though it is well known that AH should be well controlled, still is suboptimally treated in patients with DM2 indicating that physicians are reluctant to increase the number of drugs used. However, the majority of DM2 patients are using an ACEI or ARB as recommended.

Keywords: Type 2 diabetes mellitus; Hypertension; Drug therapy; Achieving target for blood pressure

PO-100

PREVALENCE OF METABOLIC SYNDROME ACCORDING TO DIFFERENT DEFINITIONS IN A MEDITERRANEAN COHORT OF HYPERTENSIVES

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Aims: The metabolic syndrome (MetS) is associated with increased risk for cardiovascular disease (CVD) and diabetes mellitus (DM). Several definitions of MetS have been proposed. The aim of the present study was to estimate and compare the prevalence of MetS according to the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III), American Heart Association - National Heart Lung and Blood Institute (AHA-NHLBI), International Diabetes Federation (IDF) and recent Joint Interim Statement (JIS) definitions in patients attending a hypertension clinic.

Methods: The records of patients referred to the Hypertension Clinic at the University Hospital (Heraklion, Crete) from January 2001 to June 2009 were screened retrospectively. A total 384 patients (146 men) were included in the study.

Results: The prevalence of MetS according to the IDF and JIS definitions was significantly higher compared with that of the NCEP ATP III in both genders (IDF: $P = 0.009$ and $P = 0.002$, JIS: $P = 0.002$ and $P = 0.001$ for men and women, respectively); this was the case for the AHA-NHLBI definition only among women ($P = 0.03$). All MetS components differed significantly (P from <0.0001 to 0.02) between patients with and without MetS for all definitions.

Conclusions: The prevalence of MetS varies considerably depending on the definition used in a hypertensive population in a Mediterranean country. These differences will influence risk assessment.

Keywords: Metabolic syndrome; Hypertension; Cardiovascular disease

PO-101

TELMISARTAN PROPHYLACTIC TREATMENT INDUCES TISSUE-SPECIFIC GENE MODULATION FAVORING NORMAL GLUCOSE HOMEOSTASIS IN CRDH RATS

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Background: Hypertension and type II diabetes are a frequently occurring co-morbidity that carries a major risk of cardiovascular complications. The Cohen Rosenthal Diabetic Hypertensive (CRDH) rat is a model of this dual pathology and a unique tool to evaluate potential monotherapies targeting both diseases. Telmisartan, an AT1R antagonist and PPARγ partial agonist, ameliorates hypertension and hyperglycemia in animal models and humans.

Purpose of Study: This study intended to determine whether prophylactic treatment with telmisartan prevents the onset of both diseases in CRDH animals, and whether changes in the expression of genes in fat, liver and muscle, the three major targets of insulin action, are a possible mechanism of the drug's antihyperglycemic action.

Materials and Methods: CRDH rats were chronically treated with telmisartan (3 mg/kg/day), starting at age 6–8 weeks before developing hypertension or diabetes. Weight changes, blood pressure, blood insulin, adiponectin, glucose tolerance and insulin sensitivity were monitored. Fat, liver, and muscle mRNAs were examined for the expression of genes potentially involved in the onset of insulin resistance.

Results: Telmisartan prevented the development of hypertension and diabetes, evidenced by blood pressure, glucose tolerance and insulin sensitivity levels close to those of non-hypertensive, non-diabetic controls. The expression of mRNAs for PPARα, PPARγ, PPARδ, APPL1, adiponectin, adiponectin receptors-1 and-2, AMPK, and GLUT4 was tissue specific and exhibited tissue-specific changes upon developing hypertension-diabetes comorbidity, particularly in fat.

Conclusion: Prophylactic treatment with telmisartan prevented most of these changes, suggesting that its primary target is fat and that its action is mediated through gene regulation of adiponectin and its downstream effector genes.

Keywords: CRDH; Telmisartan; PPARgamma; PPARdelta

PO-102

HYPERURICEMIA AND THE PATHOGENESIS OF HYPERTENSION AND INSULIN RESISTANCE IN MURINE MODEL OF THE METABOLIC SYNDROME

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Objective: Hyperuricemia is strongly associated with obesity and the metabolic syndrome and can predict visceral obesity and insulin resistance. Previously, we showed that soluble uric acid directly stimulated the redox-dependent proinflammatory signaling in adipocytes. Here we demonstrate the role of hyperuricemia in the production of key adipokines, insulin resistance and hypertension.

Research Design and Methods: We used mouse 3T3-L1 adipocytes, human primary adipocytes and mouse model of metabolic syndrome and hyperuricemia.

Results: Uric acid induced in vitro an increase in the production (mRNA and secreted protein) of monocyte chemotactic protein-1 (MCP-1), an adipokine playing an essential role in inducing the proinflammatory state in adipocytes in obesity. In addition, uric acid caused a decrease in the production of adiponectin, an adipocyte-specific insulin sensitizer and anti-inflammatory agent. This effect could be prevented by antioxidants or activation of PPAR-gamma. In obese mice with metabolic syndrome ('Pound' mice), we observed hyperuricemia, hypertension, and insulin resistance. Lowering uric acid in these mice by inhibiting xanthine oxidoreductase with allopurinol could improve the proinflammatory endocrine imbalance in the adipose tissue by reducing production of MCP-1 and increasing production of adiponectin. In addition, lowering uric acid in obese mice decreased macrophage infiltration in the adipose tissue as well as reduced insulin resistance and blood pressure.

Conclusions: Hyperuricemia might be partially responsible for the proinflammatory endocrine imbalance in the adipose tissue, which is an underlying mechanism of the low-grade inflammation and insulin resistance in subjects with the metabolic syndrome. By improving endocrine balance, lowering uric acid levels improved insulin sensitivity and blood pressure.

Keywords: Uric acid; Adipose tissue; Adipokine; Metabolic syndrome

New Insights into the Role of Uric Acid in Hypertension

PO-103

RELATION OF URIC ACID WITH BLOOD PRESSURE AND HEALTH RELATED QUALITY OF LIFE 1 YEAR POST MYOCARDIAL INFARCTION

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The purpose of the study was to assess the possible relationship of uric acid (UA) at admission with blood pressure (BP) and health related quality of life (HRQoL) 1 year after acute myocardial infarction (AMI) as onset manifestation of coronary artery disease (CAD). The sample consisted of 112 AMI survivors who satisfied all inclusion criteria and consented to participate during the 1 year post-AMI follow up. HRQoL was measured with a generic and a disease specific instrument, the 15D and the MacNew respectively. UA showed moderate correlations with EF, BMI, glucose, creatinine and proBNP (Pearson r: 0.41, −0.42, 0.50, 0.41, 0.53, 0.54 respectively with $P < 0.01$). Patients were divided into 4 groups: (1) taking allopurinol, (2) UA<3 mg/dL, (3) UA:3–6 mg/dL and (4) UA > 6 mg/dL. ANOVA revealed differences between groups, generally in favor to group (3), in terms of systolic BP, age, HR, BMI, EF, HCT, glucose, urea, creatinine, K and proBNP. As for HRQoL, group (3) reported higher levels with both instruments. Additionally, differences between the groups were observed in terms of gender, method of revascularization, and major CAD risk factors. In conclusion, AMI survivors with admission UA:3–6 mg/dL demonstrated better BP control and higher level of HRQoL. Despite the presence of not adequate controlled confounding factors, the results support the increasing evidence of the significant relation of UA to hypertension and cardiovascular disease.

Uric acid subgroups: BP, HRQoL and other parameters

Parameter	Group A (n:9)	B (n:17)	C (n:72)	D (n:14)	p
Blood pressure					
SBP	119	135	121	136	**
DBP	76	74	74	77	ns
PP	43	60	48	59	**
MBP	97	105	98	106	**
HRQoL					
15D	,807	,797	,856	,838	*
MN *emotional*	5,5	5,5	5,6	5,4	ns
MN *physical*	5,0	5,1	5,6	5,4	*
MN *social*	5,2	5,5	5,7	5,6	ns
MN *global*	5,3	5,3	5,5	5,3	ns
HR	77	65	66	69	*
CRP	6,0	4,8	4,1	4,4	ns
ESR	14	17	20	29	ns
proBNP	2079	778	1268	1558	**
EF	55	64	57	50	**
BMI	29,8	26,9	29,3	31,9	**
AGE	73,9	65,2	62,9	64,4	*
Gender					*
Male	6	10	61	8	
Female	3	7	11	6	
Cad risk factors					
Hypertension	9	14	34	12	**
Dyslipidemia	4	13	33	8	ns
Diabetes	4	5	10	8	**
Smoking	0	12	35	0	**
Family history	0	4	11	8	**
Revascularization method					*
None	0	3	11	0	
PCI	6	9	44	4	
CABG	3	5	17	10	
Glucose	225	136	137	193	**
Urea	49	32	39	53	**
Creatinine	1,22	0,89	1,06	1,25	**
K	4,2	4,2	4,4	4,6	**
Na	141	140	140	140	ns
Uric acid	7,6	3,0	4,8	7,4	**
HCT	42	43	43	39	**

*$P < 0.05$, **$P < 0.01$.

Keywords: Uric acid; Hypertension; Quality of life; Myocardial infarction

PO-104

HYPERTENSION IN HYPERURICEMIC GOUT SUBJECTS RECEIVING FEBUXOSTAT OR ALLOPURINOL

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Elevated serum urate (sUA) is an independent risk factor for hypertension (HTN).[1] We retrospectively analyzed changes in systolic and diastolic blood pressure (BP) among a subset of hypertensive subjects (N = 54) with hyperuricemia (sUA ≥8 mg/dL) and gout who received a xanthine oxidase inhibitor, febuxostat (FEB) or allopurinol (ALLO), for ≥28 weeks, and were not taking antihypertensive medication at baseline or during the treatment period. Subjects were enrolled in 1 of 3 Phase 3 randomized, double-blind, controlled studies—APEX, FACT, or CONFIRMS. The treatment groups common to each of the 3 studies, daily FEB (80 mg) and ALLO (100–300 mg, depending upon renal function status) are included in this analysis. Subjects with seated cuff BP measurements taken both prior to dosing and at Week 28 are included. HTN was defined as baseline systolic BP (SBP) ≥160 mmHg and diastolic BP (DBP) ≥95 mmHg. The change from baseline to Week 28 for DBP and SBP was calculated for each subject and summarized.

This subset of subjects receiving FEB 80 mg experienced significant reductions in both SBP and DBP from baseline by Week 28; subjects receiving ALLO experienced significant reductions in DBP (Table; $P < 0.05$). These findings suggest a possible additional benefit for sUA lowering in hypertensive patients with hyperuricemia and gout. Further studies are needed to confirm this benefit.

Reference: 1. Sundstrom J, et al. Hypertension. 2005;45:28-33.

Table I. Mean BP at Baseline, Week 28, and change from baseline among a subset of subjects with hypertension and not on anti-hypertensive treatment at baseline.

		Febuxostat 80 mg		Allopurinol 100/300 mg	
	Week	N	Mean mmHg	N	Mean mmHg
SBP	BL	29	147	25	144
	28	29	138	25	140
	Mean Δ		-9.5		-4.5
DBP	BL	29	94	25	98
	28	29	86	25	88
	Mean Δ		-8.4		-9.4

Keywords: Hypertension; Hyperuricemia and gout; Urate-lowering therapy; Febuxostat

Pediatric Hypertension

PO-105

SYSTOLIC AND DIASTOLIC BLOOD PRESSURES AMONG SICKLE CELL PATIENTS

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Background: Stroke is a well recognized complication of sickle cell disease with 11% of patients having a stroke before the age of 20. The Cooperative Study demonstrated an increase risk of stroke with increased systolic blood pressure; however, the role of diastolic blood pressure is unknown. The objective of this study is to provide a profile of blood pressure levels among patients with sickle cell disease (SCD).

Methods: The study data base derived from the Stroke Prevention Trial in Sickle Cell Anemia with an age range of 2–16, and containing 127 subjects with SCD. Systolic and diastolic blood pressure measurements were obtained at baseline, along with height and weights. Univariate and GLM analyses assessing systolic and diastolic blood pressure levels, age and body mass index were completed using SAS 9.2.

Results: For age <8 years old, the mean systolic and diastolic blood pressures were 105 mmhg [95% CL: 103–108] and 53 mmhg [95% CL: 50–55] respectively. For age ≥8 years old, the mean systolic and diastolic blood pressures were 109 mmHg [95%CL: 107–111] and 58 mmhg [95% CL: 55–60] respectively. While the systolic blood pressures were statistically similar for the two age groups, the diastolic blood pressure was significantly different. The mean BMI values was 15.1 [95% CL: 14.72–15.55] for age <8 years, and 16.3 [95% CL: 15.68–16.86] for age ≥8 years. The BMI for both age groups were statistically different. Age was the only significant variable (P value = 0.0354) in the multiple linear regression model for the cohort. BMI was not significant predictor for diastolic blood pressures.

Conclusions: These results suggest the profile of diastolic blood pressure might be different for children and adolescent with sickle cell disease compared with their counterparts without the disease. When compared to national baseline charts, the mean systolic and diastolic blood pressure was greater in sickle cell patients. In particular, body mass index was not a significant predictor of blood pressure level. Further analysis is needed to determine the exact association between age and diastolic blood pressure.

Keywords: Sickle cell disease; Stroke; Blood pressure.

PO-106

ANTIHYPERTENSIVE DRUG USE IN CHILDREN: ARE THE DRUGS LABELED AND INDICATED?

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As a result of several legislative initiatives, including the Food and Drug Administration Modernization Act (FDAMA) and Best Pharmaceuticals for Children Act (BPCA), the number of pediatric clinical trials and medications with FDA-approved pediatric labeling has increased substantially. To assess the success of these initiatives, we examined the degree to which antihypertensive drugs used by hypertensive children in 2008 had FDA-approved pediatric labeling and indications.

Using a commercial insurer database with approximately 20 million covered lives (including 1.5 million children) representing all regions of the United States and a wide range of pediatric providers, we identified 2915 patients (age<18 years) with primary (n = 2.607) and secondary (n = 308) hypertension using Episode Treatment Groups. Pharmacy claims were extracted to calculate drug user rates and days of supply. Drugs were categorized based on pediatric labeling and indication, and whether recommended for pediatric use in the National High Blood Pressure Education Program Fourth Report.

889 (34%) of primary hypertensive patients and 200 (65%) of secondary hypertensive patients were treated with an antihypertensive drug. User rates were significantly lower in

children aged 6-<12y (30.9%) than in those <6y (44.3%) and those 12-<18y (38.1%) (0-<6 vs 6-<12, $P = 0.001$; 12-<18 vs 6-<12, $P = 0.01$). Overall, 7% of drugs used were neither labeled for pediatric use, nor considered recommended for use in children in the Fourth Report. In children <6 years old, 29% of drugs used had FDA-approved pediatric label information, but were not indicated for use in that age group.

These data show that despite recent legislative initiatives, many drugs used by hypertensive children still lack appropriate pediatric labeling. Additional efforts are needed to close the gap between the availability of drugs that are labeled and indicated for pediatric use and actual drug usage in children.

Keywords: Children; Adolescents; Health policy; Antihypertensive medications.

PO-107

CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF CHILDREN WITH HYPERTENSION (HTN): NEW MULTICENTER DATA

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Most available information on the characteristics of children and adolescents with HTN comes from single-center reports. To gain better understanding of the demographic and clinical characteristics of hypertensive youth in the current era, we examined baseline data on 351 children aged 1–16 years old who had been enrolled in 2 multicenter trials of valsartan conducted in 81 centers in 13 countries.

Anthropometric, laboratory and demographic information at the time of randomization was extracted from the clinical trials database of the 2 studies. Summary variables were created and compared for 3 age groups: 1-<6 years ($n = 90$), 6-<12 years ($n = 131$) and ≥12 years ($n = 130$). Comparisons were also made between different etiologies of HTN (primary vs secondary), and for different anthropometric categories (obese vs non-obese).

Selected comparisons between the age groups are summarized in the Table: Systolic (S) and diastolic (D) blood pressure (BP) index were similar across age groups for those with secondary HTN, but SBP index was significantly higher in the 6-<12y and ≥12y groups than in the 1-<6y group for those with primary HTN. Obesity had no significant effect on SBP or DBP index.

We conclude that young children are more likely to have secondary HTN, have higher diastolic BP index and lower GFR, and are less likely to be obese or have elevated cholesterol than school-age children or adolescents. As expected, there was little variability in HTN severity in this clinical trial population. These findings emphasize unique aspects of childhood HTN that should be considered when evaluating children and adolescents with elevated BP.

Characteristic	1-<6y	6-<12y	≥12y	*P*
Secondary HTN (%)	83	38	40	<0.0001
Male (%)	60	56	65	NS
Prior drug therapy (%)	71	59	67	NS
Weight >95 percentle (%)	17	48	50	<0.0001
BMI >95 percentile (%)	16	52	52	<0.0001
Schwartz GFR (ml/min/1.73m2)	90.9 ± 31.8	141.4 ± 42.1	138.3 ± 46	<0.0001
Total cholesterol >95 percentile (%)	8	21	16	0.04
Mean SBP index*	1.1 ± 0.07	1.1 ± 0.07	1.1 ± 0.07	NS
Mean DBP index*	1/1 ± 0.15	1.0 ± 0.14	1.0 ± 1.06	<0.001

*BP index = subject BP/95th percentile

Keywords: Children; Adolescents; Obesity; Secondary hypertension.

PO-108

CARDIOVASCULAR RISK FACTORS IN OBESE CHILDREN AND ADOLESCENTS

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The association between overweight and cardiometabolic risk factors has been reported in adults, but very little is known about this association at paediatric age.

Objective: To assess the prevalence of cardiometabolic factors overweight children and adolescents. Design and Method. Two hundred and ninety overweight, Caucasian children and adolescents of both sexes, of European origin from 6 to 18 years of age (mean age 10.92.8, 160 men), were selected. Subjects with BMI from the 85th to 97th percentile were defined as overweight, those higher than 97th as obese. A validated oscillometric method was employed to measure ambulatory BP (Spacelabs 90207) during 24 hours. Fasting glucose and insulin were measured, and the HOMA index (HI) was calculated. Lipid profile was also assessed. Hypertension and metabolic abnormalities were defined following the ESH Guidelines in Children and Adolescents (J Hypertens, 2009). Insulin resistance was considered when HOMA index was >/= 4.5. The number of cardiometabolic risk factors associated to overweight was assessed by multiple regression analysis.

Results: The prevalence of cardiometabolic risk factors was: 1) Office HTN 2.8% and ambulatory HTN 11.8% (isolated SBP 19 cases, isolated DBP 3 cases and SBP-DBP HTN 12 cases). High HOMA index 33%. 3) Hypercholesterolemia 5.1%. 4) HypoHDL 0.7%. 5) Hypertriglyceridemia 10.5%. The percentage of subjects with one or more risk factors associated to overweight was one factor 33%, two factors 8.6%, three 1.7% and four 0.3%. Factors associated to the number of clustered cardiometabolic risk factors were BMI z-score ($P < 0.001$) and age ($P < 0.001$) in a multivariante analysis. Hypertension was associated with a high prevalence of abnormal HOMA index as well as hypercholesterolemia and hypertriglyceridemia. Abnormal HOMA index was associated with hypertriglyceridemia.

Conclusions: Practically half of the overweight children and adolescents have one or more cardiometabolic risk factors. The association is greater in subjects with hypertension as compared to the normotensives. The potential impact of overweight in cardiovascular disease is operating early in life.

Keywords: Children and adolecents; Obesity; Cardiovascular risk factors.

PO-109

LEFT VENTRICULAR GEOMETRY IN CHILDREN WITH PRIMARY HYPERTENSION: PREVALENCE AND PREDICTORS

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In adults, abnormal left ventricular geometry confers a similarly increased cardiovascular (CV) risk whether or not left ventricular hypertrophy (LVH) is also present. While LVH is known to be

present in up to 40% of hypertensive children, and may be more common in AA children than non-AA children with primary hypertension (PHTN), little is known about the prevalence of abnormal LV geometry among children with PHTN, or about the role of race on the presence of abnormal LV geometry.

We conducted a cross-sectional study of 104 children aged 3–21 seen at 3 tertiary medical centers from 1995 to 2005 for initial evaluation of high BP and ultimately diagnosed with PHTN. Children were categorized as having (1) normal geometry; (2) concentric remodeling (relative wall thickness (rwt)≥0.41 + no LVH); (3) eccentric hypertrophy (rwt<0.41 + LVH); (4) concentric hypertrophy (rwt≥0.41 + LVH); (5) abnormal geometry not specified (rwt missing + LVH). Chi-squared analyses were utilized to determine racial differences in the prevalence of abnormal LV geometry. Multivariate logistic regression (MLR) analysis was conducted to determine the odds of abnormal geometry by race, adjusting for age, sex, BMI z-score and BP.

Among all children, 53% had abnormal geometry. Stratified by race, 71% of AA and 47% of non-AA children had abnormal geometry (P = 0.02). MLR revealed that AA children had an 11.4 times increased odds of abnormal LV geometry compared to non-AA (P = 0.009). While BMI z-score was not associated with abnormal LV geometry in AA children (OR 0.95 (P = 0.9)), each 1 unit increase in BMI z-score was associated with a 2.4 times increased odds of abnormal geometry in non-AA children (P = 0.002).

Abnormal LV geometry is highly prevalent among children with PHTN at initial presentation. The burden and odds of having this additional CV risk factor was significantly higher in AA compared to non-AA children. These findings, along with the differential effect of BMI z-score on LV geometry by race, have not been previously described. They suggest that all children with PHTN may be at increased CV risk than was previously understood, and that race may play an important role in the development of target organ damage among children with PHTN.

Keywords: Left ventricular geometry; Pediatric primary hypertension; Racial differences in LV geometry; Clinical hypertension

PO-110

SERUM URIC ACID IN US ADOLESCENTS: DISTRIBUTION AND RELATIONSHIP TO DEMOGRAPHIC CHARACTERISTICS AND CARDIOVASCULAR RISK FACTORS

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Objective: Despite being associated with multiple disease processes and cardiovascular outcomes, uric acid (UA) reference ranges for adolescents are lacking. We sought to describe the distribution of UA and its relationship to demographic, clinical, socioeconomic, and dietary factors among US adolescents.

Patients and methods: A nationally representative subsample of 1,912 adolescents 13–18 years in NHANES 2005–2008 representing 19,888,299 adolescents was used for this study. Percentiles of the distribution of uric acid were estimated using quantile regression. Linear regression models examined the association of UA and demographic, clinical, socioeconomic, and dietary factors.

Results: Mean UA level was 5.14 ± 1.45 mg/dl. Mean UA increased with increasing age and was higher in non-Hispanic white race, male sex, higher BMI Z-score (BMI), and with higher systolic blood pressure. 273 children (15.8%) had elevated blood pressure. Of these, 50 (2.9%) were hypertensive and 223 (12.9%) were pre-hypertensive. UA levels were not significantly different between the pre-hypertensive and the hypertensive groups. Systolic BP, and classification as hypertension/pre-hypertension were significantly associated with increasing UA quartile (P = 0.019 and <0.001, respectively. In fully adjusted linear regression models, sex, age, race, and BMI were independent determinants of higher UA. C-reactive protein and poverty had a "J-shaped" relationship with UA, while albuminuria was related to lower UA levels.

Conclusion: This study helps to define serum uric acid reference ranges for adolescents. Our data also reveal some intriguing relationships between serum UA and demographic and clinical characteristics that warrant further studies to examine the pathophysiological role of UA in different disease processes.

Keywords: Uric acid; Adolescence; Blood pressure; Racial differences

PO-111

CLINIC AND AMBULATORY BLOOD PRESSURE MEASUREMENTS AND PATTERNS IN ASYMPTOMATIC CHILDREN WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is an inflammatory condition associated with multiple comorbidities and affects multiple tissues including the cardiovascular endothelium. Normative blood pressure (BP) data is lacking and the prevalence of hypertension and abnormal blood pressure patterns remains unknown in children with sickle cell disease.

Objective: To 1) Compare clinic BP and 24 hour ambulatory blood pressure (ABP) in our cohort to the 4th report and ABP normative data. 2) Examine the correlation between clinic BP and ABP. 3) Examine ABP patterns. 4) Describe the prevalence of abnormal BP and 5) Examine factors associated with abnormal BP in a cohort of children with SCD.

Design/Methods: Using a cross sectional study design, 22 asymptomatic children with SCD underwent 24 hr ABP monitoring. Average of second and third clinic BP measurements was used to calculate clinic BP index, systolic and diastolic ABP index were calculated. Medical records were reviewed and history of pain, vaso-occlusive disease, sickle cell genotype, medications, and family history of hypertension were recorded. Two measurements of urinary microalbumin to creatinine were obtained.

Results: Twenty-two children were enrolled with a mean age 13 2.9 years, BMI 20 3.4, 13 were male, 59% had HbSS, and 36% were on chronic transfusion therapy.

Mean clinic SBP and DPB indexes were 0.88 0.08 and 0.78 0.12, repectively with 13.6% being hypertensive, on the other hand, mean 24 hr ambulatory SBP and DBP indexes were 0.98 0.09 and 0.9 0.09, respectively with 36.3% being hypertensive.

Our cohort had impaired SBP dipping (7.2 6.6%) with 22.7% having reversed dipping.

Clinic and ABP systolic and diastolic indexes were modestly correlated, rho= 0.46 (P = 0.03) and rho= 0.49 (P = 0.02), respectively.

Conclusions: Abnormalities in BP measurements and patterns in children with sickle cell disease require more attention from heath care providers. ABPM is a valuable tool in identifying

masked hypertension and abnormalities in diurnal BP. Large studies are needed to identify subgroups of sickle cell patients at higher risk of BP abnormalities.

Keywords: Ambulatory blood pressure; Clinic blood pressure; Sickle cell disease; Pediatrics

Risk Factors (Lipids)

PO-112

EVALUATING THE EFFECTS OF HYPERCHOLESTEROLEMIA ON VASCULAR RISK PROFILE OF TREATED HYPERTENSIVE PATIENTS. RESULTS OF A CROSS-SECTIONAL NATIONAL STUDY

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Aim: To evaluate the effects of hypercholesterolemia (treated or not treated) on vascular risk profile of hypertensive patients.

Material and methods: Using data of 68045 hypertensive patients selected from the Spanish Hypertension Society Registry on ABPM, we compared 9805 (14.41%) hypertensive hypercholesterolemic (HCH) patients (LDL-ch $\geq$ 160 mg/dl or less with statins) (64.1 years old, 53.7% males and mean BMI 29.5 kg/m2), vs 58240 treated hypertensive normocholesterolemic (59 years old, 53.1% males, mean BMI 28.9 kg/m2) patients (HNC). To estimate the vascular risk, the 2007 ESH-ESC guidelines were applied.

Results: (HHC vs HNC) Mean Office BP (mmHg): 150.5/87.7 vs 149.2/84.7 ($p < 0.001$). Prevalence of concomitant vascular risk factors and TOD (%): Diabetes 35.2 vs 17.1, Obesity 40.7 vs 35.4, Smoking 13.2 vs 17.0 ($P < 0.001$), Microalbuminuria 11.8 vs 4.5, LVH 14 vs 6.6, Carotid Atherosclerosis 9.1 vs 3.6 (For all $P < 0.001$). CV complications: (%) Stroke 9.3 vs 3.3, IHD 16 vs 5, CHF 3.1 vs 1.7 and CKD 4.5 vs 1.5 (For all $P < 0.001$). Patients with high or very high vascular risk 74.4 vs 40.8 ($P < 0.001$).

Conclusion: Hypercholesterolemia seems to negatively influence the vascular risk profile of treated hypertensive patients. We must intensify treatment and control of dyslipidemia among hypertensive patients.

Keywords: Hypercholesterolemia; Hypertension; Vascular risk.

PO-113

NEGATIVE INFLUENCE OF HYPERCHOLESTEROLEMIA ON BLOOD PRESSURE CONTROL. RESULTS OF A SPANISH NATIONAL SURVEY WITH ABPM

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Aim: To compare the degree of 24 hours BP control between Hypercholesterolemic hypertensive (HCH) and hypertensive normocholesterolemic patients (HNC).

Material and methods: Using data of 68045 hypertensive patients from the Spanish Hypertension Society Registry on ABPM, we compared the degree of clinic and 24-h BP control on 9805 (14.41%) HCH (LDL-ch $\geq$ 160 mg/dl or less with statins) (64.1 years old, 53.7% males and mean BMI 29.5 kg/m^2), vs 58240 (59 years old, 53.1% males, mean BMI 28.9 kg/m^2) HNC patients. ABPM was performed under standardized conditions and conventional threshold for ABP measurements.

Results: (HHC vs HNC) Mean BP (mmHg): Office: 150.5/87.7 vs 149.2/84.7 ($P < 0.001$), 24h: 129.9/76.9 vs 127.5/73.5, Daytime: 133/79.7 vs 132/76 ($P < 0.001$) and Nighttime 122.5/67 vs 121/66 ($P < 0.001$). BP control (HHC vs HNC) (%); 24h: 49.6 vs 53.4, Daytime: 57.3 vs 60 ($P < 0.001$) and Nighttime: 41.3 vs 41.7 (ns). Non dipper patterns (%): 61.5 vs 53.3 ($P < 0.001$). Mean antihypertensive drugs: 2.1 vs 1.3 ($P < 0.001$). Combination therapy 71.3 vs 59.5% ($P < 0.001$)

Conclusion: In spite of a more intensive antihypertensive treatment, HCH patients show a poorer BP control than HNC patients. Hypercholesterolemia may be considered as a factor hindering BP control.

Keywords: Hypercholesterolemia; ABP monitoring

PO-114

ASSOCIATION OF WEIGHT MISPERCEPTION WITH ABNORMAL LIPID LEVELS AND HYPERTENSION AMONG OVERWEIGHT AND OBESE REPRODUCTIVE-AGE WOMEN

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Weight misperception (overweight and obese individuals who consider themselves as normal weight) is very common among reproductive-age women. However, its impact on health including its association with an abnormal lipid profile or hypertension has not been investigated. We analyzed body weight, height, waist circumference (WC), lipid profile, systolic and diastolic blood pressure, self-reported hypertension and antihypertensive drug use, and self-perception of body weight data obtained from 5,961overweight and obese reproductive-age women (16–49 y) as part of the National Health and Nutrition Examination Survey (NHANES) between 1999–2008. Multivariable logistic regression analyses were used to examine the association of weight misperception with abnormal blood cholesterol, triglyceride, and waist circumference after adjusting for age, body mass index, education level, race/ethnicity, and survey period. Twenty-four percent (1416/5961) of overweight and obese women underestimated their body weight and considered themselves as normal weight. In total, 41% of overweight and obese women had an abnormal total cholesterol (TC) level ($\geq$200 mg/dL), 32% an abnormal triglyceride (TG) level ($\geq$150 mg/dL), and 84% an abnormal waist circumference (>88 cm). Compared to accurate perceivers (those who perceived their body weight as overweight or obese), misperceivers were more likely to have abnormal values for TC (odds ratio (OR) 1.61, 95% confidence intervals (CI): 1.35–1.91), low-density-lipoprotein cholesterol (OR 1.44, 95% CI: 1.10–1.88), TG (OR 2.00, 95% CI: 1.54–2.60), and WC (OR 1.29, 95% CI: 1.01–1.64) and less likely to have an abnormally low density lipoprotein cholesterol (OR 0.73, 95% CI: 0.56–0.96). No significant differences were observed with regard to hypertension. The higher likelihood of abnormal lipid levels among overweight and obese misperceivers we observed is a public health concern. More research needs to be done to investigate several mediators that could account for the relationship between weight misperception and abnormal lipid level. Clinicians should provide patient-specific counseling related to weight misperception and its obesity related consequences.

Keywords: Weight misperception; Overweight and obese; Reproductive-age women; Serum lipid level

PO-115

INFLUENCE OF METABOLIC SYNDROME COMPONENTS IN ATHEROSCLEROTIC DISEASE AND INTIMA MEDIA THICKNESS OF CAROTID ARTERY ASSESSED BY GRAY SCALE METHOD

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Introduction: Increased intima media thickness (IMT) and metabolic syndrome have been considered an early marker of coronary atherosclerosis and is associated cardiovascular disease. The aim of this study was to evaluate a potential association between the echogenicity of IMT and cardiovascular risk factors and to evaluate if any change in echogenicity would be better correlated with metabolic syndrome components than IMT itself.

Methods: We evaluated 80 men aged from 30 to 60 years old, where 60 had previous diagnosis of high blood pressure with (n = 30) or without (n = 30) metabolic syndrome and 20 were control subjects. Patients had their anthropometric and blood pressure measures obtained prior to bloos tests. Blood samples were drawn to check the presence of metabolic syndrome (fasting glucose, total cholesterol, HDL-C, LDL-C and tryglicerides), in addition to uric acid and C-reactive protein. Carotid arteries were evaluated bilateraly by B-mode ultrasound techique and the exam was performed by a blinded examiner regarding patient's status. Gray scale method (GSM) was applied in all carotid IMT measures using a computer system.

Results: The mean age of study population was: 49.1 ± 6.9. We did not find any correlation between GSM and age, blood pressure levels, uric acid and C reactive protein. The main result in our study was a negative correlation between GSM and waist circumference ($r = -0.28$, $P = 0.0174$) and tryglicerides ($r = -0.25$, $P = 0.03$). No correlation was found among IMT and all studied variables.

Conclusion: Our data suggest that GSM changes may be detected even before any thichening of IMT in patients with metabolic syndrome and its inverse association with visceral obesity and positive asociation with tryglicrides levels, as a part of the atherogenic dyslipidemia may lead to atherosclerotic changes earlier than we used to discuss.

Keywords: Carotid; Atherosclerosis; Computer imaging processing; Ultrasound

Stroke

PO-117

HYPERTENSION AND OTHER CO-MORBID CONDITIONS ARE NOT DETERMINANTS OF TREATMENT IN ACUTE ISCHEMIC STROKE

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Background: Stroke is the third leading cause of death in the United States. While several reperfusion treatments exist for acute ischemic stroke such as intravenous and intra-arterial thrombolytics and endovascular interventions (mechanical thrombectomy, angioplasty, and stenting) each has been employed with varying degrees of success. The co-morbidity profile and its role in determining optimal treatment for ischemic stroke is unclear. Hypertension, hyperlipidemia, diabetes mellitus, and atrial fibrillation may have a significant effect on outcomes subsequent to acute treatment in ischemic stroke.

Objective: To profile co-morbidities in ischemic stroke patients during a 12-month period and determine effect of co-morbidities on the type of treatment administered.

Methods: A retrospective analysis of ischemic stroke patients was performed to determine the co-morbidity profile and type of treatment administered. Chi-squared analysis and multiple logistic regression were used to model co-morbidities and treatment administered.

Results: The cohort for this study consisted of 402 ischemic stroke patients: 66.5% were Caucasian and 33.5% were African American, 62.6% were 65 or older. Co-morbid conditions included hypertension (59.5%), diabetes mellitus (29.1%), dyslipidemia (47.3%), and atrial fibrillation (23.4%). The proportion of patients that received reperfusion treatment was similar between Caucasians and African Americans (13.7% vs 12.9%) and between subjects less than 65 and those 65 or older (12.0% vs 14.3%). Co-morbid conditions were similar between patients receiving reperfusion treatment and patients not receiving it: hypertension (54.4% vs 60.3%), diabetes mellitus (26.3% vs 29.6%), dyslipidemia (43.9% vs 47.8%), and atrial fibrillation (26.3% vs 22.9%).

Conclusion: Co-morbid conditions are similar for ischemic stroke patients receiving reperfusion treatment and those who do not. Thus clinicians are administering procedures for ischemic stroke patients based on other determinants. Co-morbid conditions should be included in future assessments to determine their role in stroke severity.

Keywords: Ischemic stroke; Hypertension; Perfusion-computed tomography; Reperfusion.

PO-118

PROFILE OF INCIDENTAL THYROID NODULES IN 2996 PATIENTS UNDERGOING CAROTID ULTRASOUND

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The purpose of this study is to determine the incidence of incidental thyroid nodules on carotid studies in 2996 patients undergoing carotid ultrasound for clinical indication in 2009–2010.

This study is an analysis of 2996 patients who underwent carotid ultrasound at a private practice in Greenville, SC. Carotid ultrasounds were ordered for conditions including dizziness, syncope, headache, TIA, CVA, history of CAD, and carotid bruit. Patients were asymptomatic for thyroid abnormality. Incidental findings include thyroid cyst and thyroid nodules. Patients with nodules were asked to undergo thyroid scan with I-131 uptake to rule out cold nodules. Cold nodules were followed with a dedicated Thyroid Ultrasound and fine needle biopsy and open biopsy were ordered as indicated.

Among these cases, 8.34% (N = 250) had thyroid cysts and 16.05% (N = 481) had thyroid nodules. Cysts were not investigated further. Of the 2996 cases, 0.5% (N = 15) were found to be malignant. Only 0.07% (N = 2) are still undetermined.

According to SEER, the government agency responsible for tracking the incidence of cancer, the incidence of thyroid cancer in the United States is 10.2 adults for every 100,000 Americans (0.01%), much less than our finding of 0.5%. The data from our study were evaluated by an independent statistician. Our

percentage is significantly greater than the national percentage (based on Fisher's Exact Test with the p-value less than 0.001). This suggests that the actual incidence of asymptomatic thyroid cancer is much greater than the cases reported to SEER.

Given the above date, we conclude that asymptomatic incidental thyroid nodules on carotid ultrasound need further evaluation to rule out malignancy. In routine carotid studies, every effort should be made to report on incidental thyroid abnormality.

Thyroid Cancer Incidence 2009–2010 Combined						
	2009	%	2010	%	Total	%
Cases	1565		1431		2996	
Thyroid Cysts	87	5.56	163	11.39	250	8.34
Thyroid Nodules	226	14.44	255	17.82	481	16.05
Thyroid Cancers	8	0.511	7	0.489	15	0.5
Undetermined	0	0	2	0.14	2	0.07

Keywords: Thyroid; Carotid ultrasound; Cancer; Nodule

PO-119

ADDITIONAL IMPACT OF MORNING HAEMOSTATIC FACTORS AND BLOOD PRESSURE SURGE ON STROKE IN OLDER JAPANESE HYPERTENSIVES

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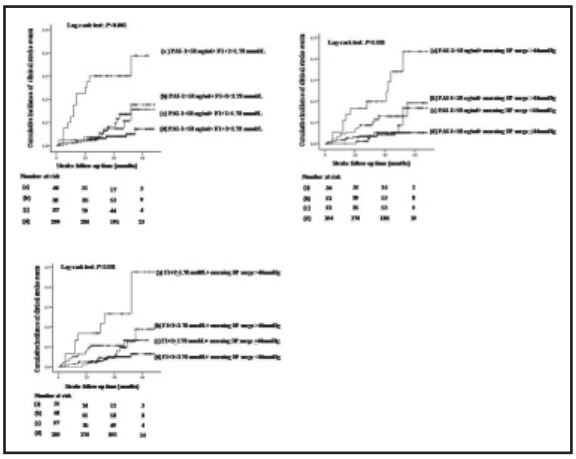
Aims: Stroke events occur most frequently in the morning hours. Impaired hemostatic activity and morning blood pressure (BP) surge, defined as the morning BP increase from sleep, have individually been associated with stroke risk in general or hypertensive populations. However, their combined impact on stroke risk remains unknown.

Methods and Results: A total of 514 hypertensive patients aged >50 years (mean 72.3 years; 37%men) underwent 24-hour BP monitoring, measurement of hemostatic risk factors (plasma fibrinogen, plasminogen activator inhibitor-1 (PAI-1), and prothrombin fragment 1 + 2 (F1 + 2)), and brain MRI at baseline. The incidence of stroke was prospectively ascertained.

During an average of 41 months (1751 person-years), there were 43 stroke events (ischemic, 30; hemorrhagic, 5; undefined, 8). On multivariable analysis adjusted for confounding factors, the hazard ratio (HR) (95%CI) for stroke in the highest vs lower quartiles of PAI-1 was 2.5 (1.3–4.6), that for F1 + 2 was 2.6 (1.4–5.0), and that for morning BP surge was 1.2 (1.1–1.4) (all $P < 0.01$). In particular, the ratio was substantially higher in cases with the highest quartile of both PAI-1 and F1 + 2 levels compared with those with the lower quartiles of both parameters (HR: 8.2; 95%CI: 3.7–18.2; $P < 0.001$). Among the patients with the highest quartile of morning BP surge (n = 128), the multivariable HR (95%CI) for the highest vs lower quartiles of PAI-1 was 3.4 (1.3–9.1) and that for F1 + 2 was 3.3 (1.3–8.7) (both $P < 0.05$). Kaplan-Meier cumulative incidences for clinical stroke events among each set of four groups are shown in Figure.



Conclusions: High levels of plasma PAI-1 and F1 + 2, as well as excess morning BP surge, are independently and additively associated with an increased risk of stroke in older hypertensive patients.

Keywords: Morning blood pressure surge; Stroke; Coagulation; Fibrinolysis

Vascular Injury/Inflammation and Remodeling

PO-120

NON-DIPPING STATUS IS ACCOMPANIED BY HYPOADIPONECTINEMIA AND INCREASED AORTIC STIFFNESS IN ESSENTIAL HYPERTENSION

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Blunted nocturnal blood pressure (BP) fall is associated with adverse cardiovascular outcome while adiponectin is an emerging marker of atherosclerosis progression. In this study we aimed to investigate the relationship of non-dipping pattern with plasma concentrations of adiponectin and aortic stiffness in essential hypertensive subjects.

148 newly diagnosed untreated non-diabetic patients with stage I to II essential hypertension [98 men, mean age=49 years, office BP=150/97 mmHg] underwent 24-h ambulatory BP monitoring and were classified as dippers and non-dippers according to the diurnal variation of >10% between mean daytime and nighttime systolic and diastolic BP. Aortic stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), using Complior SP. Metabolic profile and adiponectin levels were assessed from venous blood samples.

Non-dippers (n = 38) compared to dippers (n = 110) were older (55 ± 7 vs 49 ± 9 years, $P < 0.0001$) and had higher left ventricular mass index (119 ± 12 vs 101 ± 18 g/m^2, $P < 0.05$). In the total population, plasma adiponectin levels were negatively related with BMI (r=−0.168, $P < 0.05$), waist to hip ratio, (r =−0.421, $P < 0.0001$), office systolic BP (r r = −0.285, $P < 0.0001$), 24-h systolic BP (r = −0.194, $P < 0.05$), total cholesterol (r = −0.220, $P < 0.005$), and PWV (r=−0.280, $P < 0.001$), while it was positively associated with systolic BP fall (r = 0.520, $P < 0.001$). Additionally, PWV was associated with BMI (r = 0.233, $P < 0.05$), 24-h systolic BP (r = 0.327, $P < 0.0001$) and negatively related to systolic BP fall (r =−0.17, $P < 0.05$). Non-dippers compared to dippers exhibited attenuated adiponectin values (7.9 ± 3.6 vs 9.7 ± 4.4 μg/ml, $P < 0.05$), and higher PWV values (8.6 ± 1.2 vs 7.7 ± 4.2 m/sec, $P < 0.05$), while the two groups did not differ regarding metabolic profile (P=NS). Analysis of covariance revealed that adiponectin and PWV values remained statistically different between groups after adjustment for confounding factors ($P < 0.05$).

In essential hypertension, non-dipping pattern is accompanied by a state of increased aortic stiffening and progressive atherosclerosis,

as reflected by high levels of PWV and low levels of adiponectin, thus indicating the increased cardiovascular risk that characterizes non-dippers hypertensives.

Keywords: Non-dipping; Adiponectin; Atherosclerosis; Hypertension

PO-121

ASSOCIATION OF RETINAL MICROVASCULAR CALIBER WITH BLOOD PRESSURE LEVELS

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The most common ophthalmologic manifestation of hypertension is hypertensive retinopathy. Our study was designed to evaluate the factors that determine retinal microvacular caliber in hypertensive subjects.

During a 6-months period retinal photographs were taken from participants who underwent a routine yearly check-up. The photographs were evaluated by an ophthalmologist for hypertensive retinopathy signs, and the diameters of the individual retinal vessels were measured and summarized by a computer program. Data of the medical history, physical examination and laboratory evaluations were collected for the participants. The examiner was blinded to the medical history of the participants. The findings of the ophthalmologic examinations were related to the relevant systemic data.

We evaluated 285 subjects (43 women) with an average age of 62 ± 9 years (range 33–87). Hypertension was reported in 204 (71.6%) subjects and diabetes mellitus in 60 subjects (21%). The vascular calibers were inversely related to age. Retinal arteriolar and venular calibers were wider in smokers, and in subjects with dyslipidemia. History of hypertension was not associated with any vascular changes. However, retinal arteriolar caliber was inversely related to blood pressure levels. Diuretic treatment was associated with narrow retinal venular caliber.

The association between different cardiovascular risk factors and hypertensive retinopathy is complex. Effective blood pressure control has a beneficial effect on the vascular changes in the retina.

Keywords: Retina; Microvasculature; Blood pressure; Smoking.

PO-122

INHIBITING THE RENIN-ANGIOTENSIN SYSTEM WITH ALISKIREN AND/OR VALSARTAN PROTECTS AGAINST C-REACTIVE PROTEIN MEDIATED VASCULAR INJURY RESPONSE

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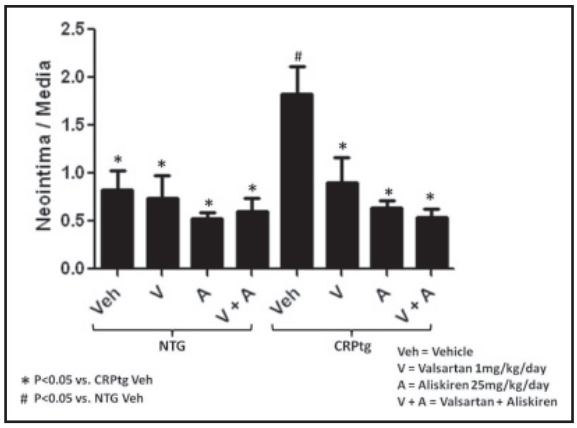
Using human C-reactive protein transgenic mice (CRPtg), we previously demonstrated that human CRP exacerbates neointima formation in response to vascular injury. We here test the hypothesis that blocking the renin-angiotensin system with the direct renin inhibitor aliskiren and/or the angiotensin receptor blocker valsartan inhibits this process.

Ovariectomized CRPtg mice were randomized to receive aliskiren (25 mg/kg/day), valsartan (1 mg/kg/day), the combination of aliskiren and valsartan, or vehicle via a subcutaneous minipump



capable of maintaining a constant level of the drug for 6 weeks. Seven days after the start of the infusion, the right carotid artery was ligated. Non-transgenic (NTG) mice served as controls. Twenty-eight days after carotid artery ligation mice were euthanized and neointima formation was determined by computer-assisted morphometric analysis of digitized images.

CRPtg mice given vehicle had an exaggerated neointimal response to injury compared to NTG given vehicle (neointima-media ratios of 1.83 ± 0.29 and 0.83 ± 0.20, respectively; $P < 0.05$). In CRPtg mice given aliskiren, valsartan, and the combination of aliskiren and valsartan the neoinitmal response was greatly diminished (0.64 ± 0.07, 0.90 ± 0.26, 0.60 ± 0.12 vs 1.83 ± 0.29, $P < 0.05$) and not significantly different from mice not expressing the human CRP transgene (0.83 ± 0.20).[figure1]Blockade of the renin-angiotensin system with aliskiren and/or valsartan ameliorates the human CRP mediated component of the vascular injury response in mice. Understanding the mechanism of this protective effect may have important therapeutic implications.

Keywords: Renin-angiotensin system; C-reactive protein; Vascular injury; Aliskiren.

PO-123

HIGH OSTEOPONTIN N-TERMINAL/C-TERMINAL FRAGMENT RATIO IS ASSOCIATED WITH CAROTID PLAQUE INFLAMMATION

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Background: The protein osteopontin (OPN) is a mediator related to atherosclerosis, hypertension and inflammation. After translation OPN is cleaved by thrombin to form an N-terminal fragment and C-terminal fragment. The N-terminal fragment is known to have an inflammatory property that exceeds those of the full length OPN. However the properties of C-terminal terminal fragment are not well characterized. The aim of this study is to evaluate whether the ratio of N-terminal/C-terminal OPN fragments correlates with plaque inflammation in hypertensive carotid atherosclerosis.

Methods: Carotid plaques were collected from 41 consecutive patients who underwent carotid endarterectomy in our institute from 2.1.2009 to 28.2.2010. After removal, the plaque was divided vertically to two fragments. One fragment was snap frozen for protein evaluation and the second fragment was

embedded in formalin. The plaques were divided to inflammatory and non inflammatory plaques according to the MQ staining. Western blot was performed for full length OPN, N- terminal and C-terminal fragments for each plaque sample.

Results: 42 atherosclerotic plaques were collected from 41 patients. The mean age of the patients was 69.25 ± 7.2 years. 27 were men and 14 women. The mean SBP and DBP were 160.6 ± 22.2 and 75 ± 12.4 respectively. There were 20 inflammatory plaques and 22 non inflammatory plaques. The abundance of OPN protein was not significantly different between the two groups. However the ratio of N-terminal OPN fragment to C-terminal fragment was nearly significantly higher in vulnerable plaques compared to the stable plaques 3.1 ± 4.6 vs 0.9 ± 1.1 respectively (*P* value = 0.06).

Conclusion: It may be suggested that the abundance of thrombin cleaved C an N OPN fragments and not the full length OPN is associated with type of plaque in hypertensive atherosclerotic patients. Higher N/C ratio is associated with carotid plaque inflammation.

Keywords: Carotid plaque; Osteopontin; Inflammation

Poster Session II
Aldosterone and Anti-Aldosterone Agents

PO-124

ALDOSTERONE METRICS AND THEIR ABILITY TO DISCRIMINATE BETWEEN INCIDENT RESISTANT HYPERTENSION DURING FOLLOW-UP IN A HYPERTENSIVE COHORT

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Resistant hypertension affects 8–30% of hypertensives. Plasma aldosterone levels are higher in patients with resistant hypertension (RH) compared to hypertensives without RH. Thus, we sought to determine whether aldosterone metrics could discriminate between hypertensives who did and did subsequently meet criteria for RH during follow-up.

The study cohort was 255 hypertensive adults (83% African American, 66% women, and median age 54 years) not meeting criteria for RH; those taking aldosterone antagonists were excluded. JNC 7 co-morbidity adjusted goal blood pressure (BP) goals were the outcomes of interest: 1) <140/90 mmHg (n = 129) and 2) < 130/80 mmHg (diabetes mellitus and/or chronic kidney disease) (n = 126). At the index clinic visit age- and sex-adjusted plasma aldosterone (ng/dL), aldosterone:renin ratio and plasma aldosterone:urine sodium ratios were contrasted between individuals with and without RH. Amongst hypertensive patients without RH at baseline (n = 76), receiver operating curves (ROC) were constructed were constructed to determine if these same three variables discriminated between those who subsequently did and did not develop RH during follow-up. The area under the curve (AUC) with 95% confidence intervals was also calculated for these six ROC curves. Two-tail p-values < 0.05 were considered statistically significant.

At the index visit, age- and sex-adjusted plasma aldosterone, aldosterone:renin ratio, and plasma aldosterone:urine sodium/urine creatinine ratio, were, respectively, 11.84 vs 12.40 (ng/dL) (P = 0.1809), 4.14 vs 5.49 (P = 0.0189) and 13.42 vs 14.43 (P = 0.009) in patients who did and did not have RH. The AUC's and 95% CI's for incident HTN amongst those with goal BP < 140/90 mm Hg were: 1) 0.72 (95% CI = 0.55, 0.89), 2) 0.61(95% CI= 0.38, 0.84) and 0.68 (95% CI= 0.475, 0.875); in those with goal BP < 130/80 mmHg, the AUC'S were 0.5 (95% CI=(0.27, 0.73), 0.47 (95% CI=(0.21, 0.73) and 0.76 (95% CI=(0.5, 1.0).

Aldosterone metrics, albeit different ones appear at different target BP levels, appear to modestly discriminate between hypertensives who develop incident HTN during follow-up.

Keywords: Resistance hypertension relationship to several different aldosterone metrics

PO-125

ALDOSTERONE-INDUCED RISE IN BLOOD PRESSURE IN NORMOTENSIVE RATS IS DUE TO A DECREASE IN PGE_2 LEVELS

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The Dahl salt-sensitive (SS) rat, but not the Dahl salt-resistant rat (SR), develops hypertension when fed a high salt diet. We have previously clearly demonstrated that salt-induced hypertension in the Dahl rat is associated with significant increases in tissue angiotensin II, aldosterone, free radical generation and endothelial dysfunction. In the present study, we extensively evaluated the direct vasculopathic effects of aldosterone (ALDO) in salt-resistant rats. We tested the hypothesis that the effect of ALDO in normotensive rats is a direct effect on vascular tissue independent of its effect when salt is present and unrelated to Ang II stimulation. Dahl salt-resistant rats fed either a low-salt (LS) or high-salt (HS) diet were treated with ALDO (0.2 mg pellet) in the presence of eplerenone (100 mg/kg/day), or apocynin (1.5 mM). Indirect blood pressure (BP) was measured prior to start of diet and weekly thereafter for four weeks. Plasma and/or tissue levels of prostaglandins (PGs) and ALDO were measured following treatment by enzyme immunoassay. Protein levels of Cox-1 and selected subunits of NADPH oxidase were assessed by western blot. Treatment with ALDO plus eplerenone, or the NADPH oxidase inhibitor, apocynin completely blocked the ALDO-induced rise in BP in both salt diet groups. This observation was accompanied with parallel changes in kidney protein levels of Cox-1, NOX4 (NADPH oxidase4) and p22phox. Plasma prostacyclin and prostaglandin E_2 levels were lower in the rats fed the high salt diet. ALDO reduced PGE_2 levels in LS fed rats compared to rats on the HS diet, which were not reversed by eplerenone and/or apocynin treatment. In contrast, the 5-fold increase in plasma thromboxane levels induced by ALDO in LS fed rats was completely blocked by eplerenone but not by apocynin. Taken together, the effects of ALDO on blood pressure and endothelial dysfunction in SR are unlike its effects on SS rats. Moreover, blocking the mineralcorticoid receptor appears to elicit a similar response as inhibiting NADPH oxidase activity; thus linking the vasculopathic effect of ALDO to this pathway.

Keywords: Aldosterone; Eplerenone; Prostaglandin E2; Normotensive

PO-126

DELAYED DIAGNOSIS OF PRIMARY ALDOSTERONISM-HELP FROM THE WEB: A YAHOO SUPPORT GROUP FOR PATIENTS STRUGGLING WITH DIAGNOSIS AND LONG-TERM MANAGEMENT

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Primary aldosteronism (PA) is the most common Endocrine cause of high blood pressure (HTN). The possibility of cure or specific drug treatment (Rx) of drug-resistant HTN (note that ACEs, ARBs and BB will not work in PA) and disabling hypokalemia (LoK) makes it rewarding to test for (Dx) this common cause of HTN. The ease of Dx (a single blood and 24 hr urine) has revolutionized the ability of the general practitioner to Dx, Rx and improve the lives of these patients. Avoiding long delays in Dx/Rx minimizes not only patient suffering but also target organ damage characteristic of this classic human model of aldosterone/salt HTN.

An online support group was organized in 2002 by a patient with the myriad problems associated with PA. This soon grew into an active support group with patients from around the world. Many have made the Dx themselves by searching the web after becoming frustrated with their health care team's failure to recognize the association of LoK and drug resistant HTN. The average pt had seen 5 different Drs before Dx.

A total of 54 patients have been given a confirmed DX of Conn's syndrome by their health care team (25 unilateral and 29 hyperplasia) and the average BP has decreased from a high of $208 \pm 35/122 \pm 24$ mm Hg before DX to $128 \pm 15/78 \pm 15$ after surgical or medical Rx 26 medical (average spironolactone Rx 60 mg or eplerenone 120/d). The average duration of poorly Rxed HTN before DX was 11 (range 1–40) years and hypokalemia 8.4 (0–58).

Based on this analysis the Dx can be easily suspected by the clinical complex: drug resistant HTN (93%), nocturia (75%), muslce cramps in 50%, and multiple ER visits for a complex of symptoms of headaches, chest pains, muscle cramps, and anxiety and finding of severe HTN and LoK (90%)

Despite the fact that the DASH diet should be a powerful adjunct treatment for aldo/salt HTN only 14% had ever had this recommended. The site stresses this and most have experienced reductions in Sx, Rx and HTN by DASHing.

We invite all who take care of difficult HTN (and their patients) to visit hyperaldosteronism at Yahoo Groups to read the files on "Conn's Stories" as we are certain they will recognize some of their own patients and be spurred to Dx and Rx PA in their own clinics. Patients will be stimulated to seek proper Dx and Rx as well by their own health care team.

Keywords: Hyperaldosteronsim; Support groups; Web based

PO-127

DOSE TITRATION OF THE ORAL POTASSIUM BINDER-RLY5016 TO MAINTAIN NORMAL SERUM POTASSIUM IN HEART FAILURE AND CHRONIC KIDNEY DISEASE PATIENTS ON ALDOSTERONE ANTAGONISTS

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Background: Chronic kidney disease (CKD) is a frequent comorbidity in heart failure (HF) and complicates or prevents the use of life-saving therapies. In the PEARL-HF trial, RLY5016 30g/d significantly reduced the incidence of hyperkalemia [HK, serum K^+ (S_K) > 5.5 mEq/L] in spironolactone (SL) treated HF patients with CKD, but also resulted in a 6% incidence of hypokalemia (S_K < 3.5 mEq/L).

Methods: To explore RLY5016 dose titration strategy to prevent HK and avoid hypokalemia, 63 patients with HF and CKD on $\geq$ 1 HF therapies (ACEIs, ARBs, or β-blockers) with mean S_K of 4.8 mEq/L and eGFR of 46 mL/min/1.73m^2 were started on RLY5016 20 g/d and SL 25 mg/d which was uptitrated to 50 mg/d if S_K was < 5.1 mEq/L. RLY5016 was titrated up/down in 10 g/d increments (0–60 g/d) with the aim of keeping S_K in the target range of 4.0–5.1 mEq/L, in order to maintain S_K in the normal range of 3.5–5.5 mEq/L (primary endpoint) during the 8 week study.

Results: All patients were up-titrated to SL 50 mg/d by Day 14. Fifty-seven patients (90%) had S_K in the normal range at study end and 48 (76%) during the entire study. One patient developed hypokalemia and 15 patients developed HK $\geq$ 1 time during the study. RLY5016 was titrated 0, 1, and $\geq$ 2 times in 32%, 21%, and 47% patients, respectively, over 8 weeks. The mean RLY5016 dose and eGFR at study end was 24 g/d and 46 mL/min/1.73m^2, respectively. Among the 21 patients with diabetes and urine albumin:creatinine ratio (ACR) > 30 mg/g, mean blood pressure (BP) was reduced from 139/84 at baseline to 129/78 mmHg ($P < 0.05$) and mean ACR from 1107 to 577 mg/g ($P < 0.05$) at week 8. Four patients (6%) were withdrawn due to moderate diarrhea (1), vomiting (1), or worsening of CKD (2). One on-treatment death (unwitnessed) occurred within 24h of a S_K 4.6 mEq/L.

Conclusions: In this HF/CKD population, on standard HF therapy, RLY5016 dose titration successfully allowed SL initiation and up-titration with maintenance of S_K in the normal range. In the subset of patients with DM and albuminuria, both BP and ACR were significantly reduced suggesting that RLY5016 may allow for the use of beneficial therapy in these high risk patients.

Keywords: Hypertension; Aldosterone antagonist; Hyperkalemia; Proteinuria

PO-128

HYPERKALEMIA WITH ALDOSTERONE ANTAGONIST MONOTHERAPY IN ESSENTIAL HYPERTENSION. A META-ANALYSIS

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Background: Spironolactone and eplerenone provide significant antihypertensive benefit when added to existing multiple drug regimens in patients with resistant hypertension. The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) showed a mean reduction 22/10 mmHg in blood pressure. Hyperkalemia occurred in 4% of the patients. However, there is still a major concern for the risk of hyperkalemia that prevents physicians from using it as a standard of care in this setting.

Methods: A PubMed and Cochrane search from randomized clinical trials was done from 1960 to November 2010. We pooled all the randomized clinical trials in which the incidence of hyperkalemia was compared head-to-head among any

aldosterone antagonists (i.e., spironolactone, eplerenone and canrenone) to another antihypertensive drug class in patients with hypertension. Studies were excluded if additional antihypertensive were added. Effect estimates were pooled across studies using random-effects meta-analysis and heterogeneity was assessed using I^2 statistics.

Results: 15 studies with a total patient population of 2714 (mean age of 54 ± 7, 55% males) were included in the analysis, 8 studies with eplerenone (50- 200mg) and 7 studies with spironolactone (25–200mg). The control groups included amlodipine (2), placebo (3), enalapril (1), nifedipine (2), chlorthalidone (1), losartan (2), propanolol (2), atenolol (1), hydrochlorothiazide (1). 14 patients out of 1479 (0.94%) had hyperkalemia on aldosterone antagonists compared to 8 out of 1158 patients (0.69%) on control/placebo, (P = 0.32). Similarly, the patient withdrawal rate due to hyperkalemia was not statistically significant (P = 0.9).

Conclusion: The incidence of hyperkalemia is very low and similar to controls when aldosterone inhibitors, either spironolactone or eplerrenone are administered as a monotherapy in hypertensive patients with normal renal function.

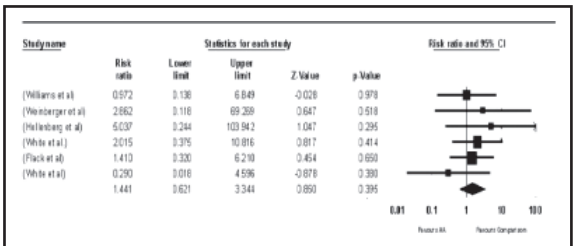

Figure 1. Head-to head comparison of aldosterone antagonists with controls/placebo. **(Studies in which incidence for both groups were "0" are not displayed).**

Keywords: Aldosterone antagonists; Hyperkalemia; Spironolactone; Eplerenone

PO-129

BODY MASS INDEX CORRELATES WITH PLASMA ALDOSTERONE IN OVERWEIGHT/OBESE HYPERTENSIVE PATIENTS DESPITE DRUG THERAPY

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Resistance to ACE inhibitors (ACEI) and angiotensin receptor blockers (ARB) long-term therapy appears to relate to a phenomenon defined as "aldosterone escape", but it is still unclear whether this relates to plasma aldosterone concentration (PAC) in treated overweight/obese (ow/ob) hypertensive patients.

The aim of this study was to evaluate the relationship between the indexes of adiposity and PAC in hypertensive, ow/ob, non-elderly patients in stable anti-hypertensive treatment.

267 consecutive essential hypertensive patients with BMI≥25 kg/m^2 referred to our centre for uncontrolled BP despite stable anti-hypertensive treatment for at least 6 months. Exclusion criteria were: age>65 years, non-caucasians, heart failure (NYHA class III-IV), LVEF<50%, GFR<30 ml/min, liver failure, malignant neoplasia, and therapy with aldosterone antagonists, amiloride or oral contraceptives. Treatment Intensity Score (TIS) was used to adjust for different drug number and dosages.

PAC was directly correlated with BMI both in unadjusted (r = 0.141; P = 0.028) and adjusted models (r = 0.287; P < 0.001). In a stepwise multiple linear regression model comprehending age, mean blood pressure (MBP), TIS, BMI, PRA, urinary Na+, fasting glucose, total cholesterol, HDL, triglycerides, LDL, eGFR, and duration of hypertension, only PRA (β=0.184; P = 0.002), MBP (β=0.153; P = 0.010), and BMI (β=0.159; P = 0.008) showed an independent correlation to PAC. In the same model applied to patients treated with ACEI or ARB, only PRA (β=0.188; P = 0.015) and BMI (β=0.230; P = 0.003) showed a direct correlation to PAC. This experimental model explained 10.5% of PAC variation in the ACEI/ARB treated subgroup. Waist circumference was correlated with PAC both in the whole population (r = 0.167; P = 0.034) as well as in the ACEI/ARB treated subgroup (r = 0.238; P = 0.014). However, when BMI was substituted by waist circumference in stepwise multiple linear regression models waist circumference was not independently associated with PAC.

In treated hypertensive patients increased adiposity, as indexed by BMI, correlates directly with PAC that is, in turn, related to mean BP. Increased adiposity and obesity may lead to higher PAC and higher BP in hypertensive patients also when on stable therapy with ACEI or ARB.

Keywords: Renin-angiotensin-aldosteron system; Obesity; Hypertension; RAS blockers

PO-130

ALDOSTERONE TO RENIN RATIO (ARR) AS A PREDICTOR OF MORTALITY AND CARDIOVASCULAR OUTCOMES

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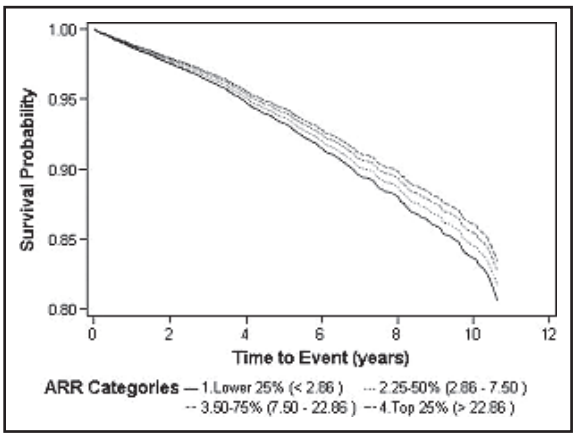
BackgroundHigher ARR is associated with resistant and refractory hypertension. We hypothesized that ARR is a predictor of death and cardiovascular events.

Methods: Historical cohort study within a large ethnically diverse outpatient population (>17 yrs) with documented ARR and minimum 1 yr follow-up. Patients were categorized into 4 ARR quartiles. Medicare and hospitalization data were used to determine death, ischemic and congestive heart event, and cerebrovascular events. Cox regression was employed to estimate hazard ratios at 2 and 5yrs after adjustment for age, gender, medication usage, hypertension, diabetes, and Charlson's comorbidity index.

Results: 4,665 subjects with documented ARR had a median follow-up of 3.4yrs and an overall 7.2% mortality. Compared to the lowest quartile of ARR, the multivariate adjusted HR (95% CI) for mortality alone at 5 yr followup was 0.86 (0.63–1.16), 0.76 (0.56–1.03), and 0.69 (0.50–0.95); and HR for combined outcomes of death and cardiovascular and cerebrovascular events were 0.94 (0.78–1.12), 0.88 (0.73–1.06), and 0.84 (0.70–1.01) for quartiles 2, 3, and 4 respectively (P = 0.05 for trend). Survival estimates (including at 2 & 5 yr) showed a similar trend toward improved survival with higher ARR.[figure1]When aldosterone and plasma renin activity were evaluated independently, aldosterone did not correlate with ARR while higher renin levels were inversely related to rising ARR and outcomes.

Conclusions: Higher ARR appears associated with lower mortality and a trend towards fewer cardiovascular and cerebrovascular events. The ARR relationship appears to be driven primarily by renin. Additional studies are to examine whether these associations are due to appropriate renin suppression or whether hyperaldosteronism is a disorder more amenable to treatment.



Keywords: Aldosterone; Renin; Hypertension; Ouctomes

Antihypertensive Drugs and Pharmacology

PO-131

BOTH MORNING AND EVENING DOSING OF NEBIVOLOL REDUCES TROUGH TO MORNING BLOOD PRESSURE SURGE IN HYPERTENSIVE PATIENTS

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Nebivolol is a third generation beta-blocker that is dosed once daily. It is unknown whether nebivolol given in the morning or in the evening will be more effective in reducing the trough to morning blood pressure surge (BPS). This randomized, placebo-controlled, cross-over study compared the effect of morning vs evening dosing of nebivolol on the trough to morning BPS. A total of 42 patients were randomized (mean age 52 ± 12 years, 52% African-Americans, and 46% females), of whom 38 completed the study. Patients were obese (body mass index 31.8 ± 5.9 kg/m2), taking an average of 1.4 antihypertensive medications, and with a mean blood pressure of 152.4 ± 11.3/92.8 ± 7.5 mmHg at the time of randomization. Both morning and evening dosing of nebivolol significantly reduced daytime, nighttime, and 24-hour ambulatory blood pressures. Further, both morning and evening dosing of nebivolol significantly reduced systolic trough to morning BPS. Nebivolol given in the morning had the added benefit of producing a larger nocturnal blood pressure fall. In patients with mild to moderate hypertension, nebivolol given in the morning or evening is effective in reducing 24 hour ambulatory blood pressure and trough to morning BPS.

Table I. 24 hour ambulatory blood pressure (BP) parameters (numbers reflect change in systolic BP [SBP] and diastolic BP [DBP] from baseline and on follow-up) for nebivolol given in the morning (AM) vs evening (PM). All BP values are expressed in mmHg.

Parameter	AM Nebivolol	PM Nebivolol
Daytime SBP	-10.0 ± 15.1 ‡	-9.8 ± 12.3 ‡
Daytime DBP	-8.3 ± 11.1 ‡	-6.9 ± 8.1 ‡
Nighttime SBP	-7.8 ± 16.6 †	-8.9 ± 17.1 *
Nighttime DBP	-6.4 ± 10.5 ‡	-6.2 ± 10.6 ‡
24-hr SBP	-9.2 ± 14.2 ‡	-9.6 ± 12.8 ‡
24-hr DBP	-7.5 ± 9.9 ‡	-6.7 ± 8.0 ‡
Trough to morning SBPS	6.8 ± 19.0 *	6.3 ± 18.5 *
Trough to morning DBPS	5.2 ± 15.1 *	3.5 ± 12.6
Nocturnal SBP Fall	8.1 ± 21.0 *	1.9 ± 18.3
Nocturnal DBP Fall	5.6 ± 14.5 *	1.7 ± 15.0

* $P < 0.05$ † $P < 0.005$ ‡ $P < 0.001$ Abbreviations used: SBPS: Systolic blood pressure surge, DBPS: Diastolic blood pressure surge

Keywords: Nebivolol; Chronotherapy; Morning blood pressure surge; Nocturnal blood pressure fall

PO-132

ADMINISTRATION-TIME-DEPENDENT EFFECTS ON AMBULATORY BLOOD PRESSURE OF HYDROCHLOROTHIAZIDE AS ADDED THERAPY IN HYPERTENSIVE SUBJECTS UNCONTROLLED WITH VALSARTAN

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Clinical studies have documented morning-evening, administration-time differences in blood pressure (BP) lowering efficacy, duration of action, safety profile and/or effects on the circadian BP pattern of different classes of hypertension medications. Only one previous study has evaluated the administration-time-dependent effects of monotherapy with a diuretic, showing a double BP-lowering efficacy when the loop-diuretic torasemide was administered at bedtime as compared to upon wakening. To obtain established BP target goals, most patients require treatment with >1 hypertension medication. Accordingly, we investigated the ingestion-time-dependent effects of hydrochlorothiazide (HCTZ) as added therapy in hypertensive subjects uncontrolled in monotherapy. We studied 204 hypertensive subjects (95 men), 49.7 ± 11.1 years of age, initially randomized to receive valsartan (160 mg/day) monotherapy either on awakening or at bedtime for 12 weeks. Due to uncontrolled ambulatory BP, HCTZ (12.5 mg/day) was added to valsartan as a single-pill formulation, maintaining the original circadian time of treatment, for another 12 weeks. BP was measured at 20 min intervals from 07:00 to 23:00 h and at 30 min intervals at night for 48 h before and after adding HCTZ. Adding HCTZ resulted in a significant reduction of the 24h BP mean, slightly greater after bedtime dosing (decrease of 6.1/4.0 mmHg in systolic/diastolic BP after HCTZ on awakening; 9.2/5.6 mmHg after bedtime dosing; P = 0.034/0.096 between groups). The efficacy of HCTZ on the awake BP mean was similar for the 2 treatment-groups ($P > 0.254$). Results, however, reveal a greater efficacy with

bedtime dosing in regulating sleep-time BP mean (decrease of 4.4/3.2 mmHg in systolic/diastolic BP after HCTZ on awakening; 9.7/6.3 mmHg after bedtime dosing; $P < 0.001$ between groups). Accordingly, there was a significant ($P < 0.001$) increase in sleep-time relative BP decline towards a more dipping BP pattern only when HCTZ was added at bedtime. In patients not properly controlled with valsartan monotherapy, the addition of 12.5 mg/day HCTZ efficiently reduces BP to a larger extent after bedtime dosing. Bedtime administration of HCTZ is also significantly more efficient than morning dosing in reducing sleep-time BP, the most relevant prognostic marker of cardiovascular morbidity and mortality.

Keywords: Chronotherapy; Combination therapy; Hydrochlorothiazide; Valsartan

PO-133

IRBESARTAN/AMLODIPINE FIXED COMBINATION IN PATIENTS UNCONTROLLED ON AMLODIPINE 5 MG (I-COMBINE STUDY)

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Objective: To compare the antihypertensive efficacy of the fixed combination Irbesartan/Amlodipine 150mg/5mg (I150/A5) to Amlodipine 5mg (A5) in lowering Systolic Home Blood Pressure Measurement (SHBPM) after 5 weeks (W5).

Methods: Multicenter, prospective, randomized, open-label, with blinded endpoint evaluation (PROBE) phase III study.
Uncontrolled patients (SHBPM $\geq$135 mmHg) after at least 1 week of A5 were randomised (1:1) in 2 parallel groups: one received I150/A5 from W0 to W5 followed by forced titration I/A 150/10 from W5 to W10; the other received A5 from W0 to W5 followed by forced titration A10 from W5 to W10.
The primary objective was the SHBPM change between the 2 groups at W5. A secondary objective was SHBPM change between the 2 groups at W10. Compliance was monitored by pill count.

Results: 403 patients in 12 countries were enrolled. ITT analysis was performed on 287 patients. Mean age was 57.3 ± 11.2 years, female 51.9%, obesity 41.8% and diabetes 15.3%. History of CV disease: 6.6%.
At W0, mean SHBPM was 148.8 ± 10.0/85.0 ± 9.2 mmHg similar in the 2 groups.
At W5, mean SHBPM were 135.9 ± 11.6 mmHg in group I150/A5 and 142.9 ± 12.2 mmHg in group A5. The adjusted mean difference between groups was -6.2 ± 1.0 mmHg ($P < 0.001$).
Percentage of controlled patients (HBPM: <135 and <85 mmHg) at W5 was 44.7% in group I150/A5 vs 21.6% in group A5 ($P < 0.001$).
At W10, after Amlodipine forced titration, mean SHBPM were 130.6 ± 11.4 mmHg in group I150/A10 and 135.4 ± 10.3 mmHg in group A10. The adjusted mean difference between groups was -4.5 ± 1.0 mmHg ($P < 0.001$).
Percentage of controlled patients (HBPM: <135 and <85 mmHg) at W10 was 67.4% in group I150/A10 vs 44.3% in group A10 ($P < 0.001$).
Compliance at W5 was 95.8% in group I150/A5 and 95.1% in group A5.
At W5, 37 (12.8%) patients (pts) experienced adverse events (AE): 20 pts in I150/A5 and 17 in A5. Most frequent AE was headache (2 pts and 5 pts in each group respectively) and oedemas (1pt and 5 pts respectively).
At W10, 46 (16.4%) patients experienced AE: 22 in I150/A5 and 24 in A5. Most frequent AE was dizziness (1 pt and 2 pts) and oedemas (7 pts and 9 pts respectively).
Per protocol analysis (130 patients in group I/A and 132 in group A) shows similar results.

Conclusion: This study shows that combination of I150/A5 achieve clinically higher BP reduction and BP control than monotherapy with A5. Forced titration of amlodipine to 10 mg in both groups induced a further BP decrease but with more AE.

Keywords: Irbesartan; Amlodipine; Fixed dose combination

PO-134

IRBESARTAN/AMLODIPINE FIXED COMBINATION IN PATIENTS UNCONTROLLED ON IRBESARTAN 150 mg (I-ADD STUDY)

Guillaume Bobrie. European George Pompidou Hospital, Paris, France.

Objective: To compare the antihypertensive efficacy of the fixed combination Irbesartan/Amlodipine 300/5mg (I300/A5) to Irbesartan 300mg (I300) monotherapy in lowering Systolic Home Blood Pressure Measurements (SHBPM) after 10 weeks (W10).

Methods: It was a multicenter, prospective, randomized, open-label, with blinded endpoint evaluation (PROBE) phase III study.
Uncontrolled patients (SHBPM $\geq$135 mmHg) after at least 1 week of treatment by I150 monotherapy were randomised (1:1) in 2 parallel groups: one received I150/A5 from W0 to W5 followed by forced titration I300/A5 from W5 to W10; the other received I150 from W0 to W5 followed by forced titration I300 from W5 to W10.
The primary objective was the change in SHBPM between the 2 groups at W10. A secondary objective was SHBPM change between the 2 groups at W5. Compliance was monitored by pill count.

Results: 436 patients from 10 countries were enrolled. ITT analysis was performed on 320 patients. Mean age was 56.7 ± 11.4 years, female 58.8%, obesity 42.2% and diabetes 20.3%. History of CV disease: 5.9%.
At W0, mean HBPM was 151.5 ± 11.0/86.3 ± 10.2 mmHg, similar in the 2 groups.
At W10, SHBPM were 133.6 ± 10.9 mmHg in group I300/A5 and 140.7 ± 13.7 mmHg in group I300; the adjusted mean changes from baseline to W10 were -19.2 ± 10.2 mmHg in group I300/A5 and -9.7 ± 10.8 mmHg in group I300. The adjusted mean difference between the 2 groups was -8.8 ± 1.1 mmHg ($P < 0.001$).
The percentage of controlled patients (HBPM: systolic <135 and diastolic <85 mmHg) at W10 was 54.1% vs 31.8% respectively ($P < 0.001$).
At W5, SHBPM were 136.8 ± 12.1 mmHg in group I150/A5 and 144.8 ± 13.6 mmHg in group I150; the adjusted mean changes from baseline to W5 were -15.4 ± 0.8 mmHg in group I150/A5 and -5.63 ± 0.8 mmHg in group I150. The adjusted mean difference between the 2 groups was -9.8 ± 1.1 mm Hg ($P < 0.001$).
The percentage of controlled patients (HBPM: systolic <135 and diastolic <85 mmHg) at W5 was 41.6 vs 22.0% respectively ($P < 0.001$).
Compliance at W10 was 100% in group I300/A5 and 99.4% in group I300.

At W10, 52 (16.0%) patients (pts) experienced adverse events (AE): 29 in I300/A5 and 23 in I300. Most frequent AE was oedemas (6 pts) in group I300/A5 and headache (4 pts) in group A5. Per protocol analysis (137 patients in group I/A and 138 in group I) shows similar results.

Conclusion: This study shows that combination of I300/A5 achieve clinically significant higher BP reduction and BP control than monotherapy with I300.

Keywords: Irbesartan; Amlodipine; Fixed dose combination

PO-135

POLY(3-HYDROXYBUTYRATE) NANOPARTICLES LOADED WITH PACLITAXEL CAUSE PROLONGED ANTIPROLIFERATIVE ACTION

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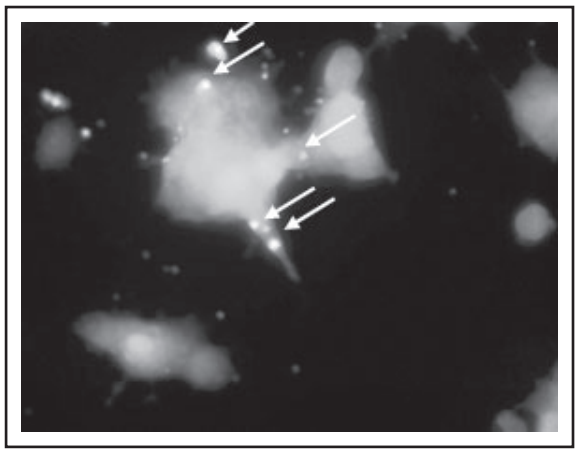
Implantation of vascular grafts and stents leads to serious shortcomings: stenosis and occlusion caused by neointimal hyperplasia. Local delivery of antiproliferative drugs may be effective to prevent this consequence while minimizing the systemic side effects they cause. The design of injectable systems on the base of nanoparticles from biodegradable polymers for sustained perivascular delivery of antiproliferative drugs is extremely challenging. We have developed composite nanoparticles (200–800 nm diameter) loaded with antiproliferative drugs, paclitaxel and etoposide. Operated composite nanoparticles were prepared on the base of a biocompatible polymer, poly(3-hydroxybutyrate) (PHB) with low molecular weight (35 kDa) that was obtained biotechnologically in framework of our original technology. We have shown that developed drug systems provide sustained drug delivery for up to 2 month in vitro. Our results demonstrated that the release of paclitaxel from the PHB matrix occurs at a uniform rate for a considerable period of time (3–45 days for PHB nanoparticles).The sustained drug release makes possible to use these systems for long-term antiproliferative action in the local site of injection. It was shown that nanoparticles loaded with paclitaxel caused inhibition of growth of MFC-7 cells during 72 hours incubation in concentration dependent manner. Moreover, the in vitro antiproliferative action of biopolymer drug system was more effective that antiproliferative action of commercially available paclitaxel drug dosage form, Taxol. We have demonstrated also by confocal microscopy an uptake of PHB nanoparticles by MFC-7 cells and sustained drug release in cytoplasm. Thus, the developed injectable biopolymer drug system is a promising technique for long-term prevention of neointimal hyperplasia. The work is supported by Federal Programme "Kadry", projects # P548, P2266, P2429.



Keywords: Poly(3-hydroxybutyrate); Nanoparticles; Paclitaxel; Neointimal hyperplasia

PO-136

THE EFFICACY AND SAFETY OF ANGIOTENSIN RECEPTOR BLOCKER AND CALCIUM CHANNEL BLOCKER COMBINATION IN HYPERTENSION

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The present study was designed to evaluate efficacy, safety and tolerability of the angiotensin receptor blocker (ARB) - calcium channel blocker (CCB) single pill combination in hypertensive patients. A total of 751 patients (62.3% female; mean age: 58.2 ± 11.1 years) under ARB-CCB single pill combination therapy were included in this non-interventional, multi center study at 170 centers in Turkey. The follow-up visits were at intervals based on the physicians' initiative. At the time of this interim analysis, 611 (81.4%), 425 (56.6%), and 139 (18.5%) patients have attended to the 1st, 2nd and 3rd follow-up visits conducted in 34.0 ± 26.0, 92.0 ± 39.0 and 157.0 ± 32.0 days after the initial visit, respectively. Average body mass index was 30.4 ± 5.3 kg/m^2 and mild obesity was seen in 39.3% of the patients. There was no past history of antihypertensive treatment in 41.9% while 21.0% were hypertensive for > 7 years. The dosage of ongoing valsartan/amlodipine combination was 160/5 mg in 42.0% of the patients, and 160/10 mg in 58.0% of patients with past history of hypertension (n = 436) most of whom (82.4%) were switched to this regimen due to insufficient efficacy of the former medication(s). The dosage of ongoing valsartan/amlodipine combination was 160/5 mg in 55.7% while it was 160/10 mg in 44.3% of patients with newly diagnosed hypertension (n = 315). Ongoing valsartan/amlodipine treatment was switched to another regimen in 10.1%, 4.7% and 5.8% of the patients at consecutive follow-ups, mostly due to insufficient efficacy (58.1%) and adverse events (19.4%). There was a significant reduction in systolic and diastolic blood pressure (mm Hg) during the follow-up visits [(138.5 ± 18.2; 84.1 ± 9.2), (133.1 ± 13.6; 82.0 ± 7.5), 131.8 ± 11.6;82.1 ± 6.9)] compared to baseline (167.9 ± 22.1; 98.7 ± 11.8) levels ($p < 0.001$ for each). Peripheral edema was present in 6.9% of patients at baseline and in 8.0%, 8.7% and 10.0% of the patients during consecutive follow-up visits. In 11.6% of the entire population, peripheral edema was evident at least one time during the study. At least one AE was reported in 8.3% of the initial patient population during the entire follow-up. In conclusion, valsartan/amlodipine single pill combination seems to be a tolerable, safe and efficient antihypertensive regimen.

Keywords: Antihypertensive treatment; Efficacy; Safety; ARB/CCB fixed dose combination

PO-137

BETTER CONTROL OF CENTRAL PRESSURES AND TOTAL HIPERTENSIVE TIME IN PATIENTS WITH HYPERTENSION RECEIVING TELMISARTAN AS MONOTHERAPHY. PROSPECTIVE STUDY

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Introduction: it is well known that mayority of hypertensive patients require more than one drug to keep their hypertension (HTA) under control. However, when we have our patients (P) treated with monotheraphy and their brachial blood pressure under 140/90 Hgmm., we consider that they are well controlled, but, we don't take into account that could be other measures such as central systolic and diastolic pressures (SCP, DCP), augmentation index (AI) and total hypertensive time (THT) which can give us better idea about the proper control of these P.

Objective: to evaluate the effects of monotheraphy with Telmisartan (TLM) or enalapril (ENA) on SCP,DCP and THT in P with HTA.

Material and methods: we studied 106 P (61 ± 8 years old, 50 women and 56 men) with HTA which were divided in two groups: group I: 66 P received 80 mg of TLM and group II: 50 P received till 40 mg of ENA. All of them had criteria of well control of their systolic and diastolic brachial blood pressure (SBBP; DBBP <140/90 Hgmm.). All of them submitted to a 24 hs., ambulatory blood pressure monitoring and to study their SCP,DCP,AI,THT.

Results: data obtained of these P we showed in the following table:

Conclusions: although we can think these P are well controlled with monotheraphy, because they had similar brachial blood pressures, we found that group I receiving TLM were better controlled because significantly their SCP, DCP,AI and THT were inferior to the group receiving ENA. We should take into account these data when we choose a treatment in these kind of P.

Results of the two groups

Data	SBBP/DBBP	SCP	DCP	THT(minute)	AI
Group I	135 ± 4/83 ± 5	102 ± 3*	78 ± 4*	156 ± 10*	21 ± 3*
Group II	138 ± 2/85 ± 5	119 ± 5	83 ± 4	385 ± 9	29 ± 2

*Means p value less than 0.05.

Keywords: Central pressure; Augmentation index; Telmisartan; Enalapril

PO-138

INTRAVENOUS HYDRALAZINE FOR BLOOD PRESSURE MANAGEMENT IN THE HOSPITALIZED PATIENT

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Background: Intravenous (IV) hydralazine has been approved for the treatment of hypertensive emergencies for 40 years. Due to the observation of increased use in the hospitalized patient, we assessed the rationale for its use and the effects of administration.

Methods: Patients (n = 94) were identified between April and October 2010 from a daily list of all hospitalized patients who had an order for IV hydralazine entered into the computerized physician order entry system. Prescribers were unaware that the study was being conducted. Demographic and clinical information, including pre-treatment blood pressure (BP), change in BP and heart rate (HR) within 2 hours post-administration of hydralazine, concurrent anti-hypertensive medications, and adverse events were obtained.

Results: Mean age was 69 ± 18 years, 48% were female and 89% had a history of hypertension. Hydralazine IV was administered 201 times at a mean dose of 11.4 ± 4.3 mg. Only 3 (3%) patients had any evidence of an urgent hypertensive condition (symptoms, target organ injury). Baseline BP was 175/82 ± 25/16 mmHg and reduced by 24/9 ± 29/15 mmHg while HR increased by 4 ± 13 beats/min. Changes from baseline in BP were evaluated according to quartiles of baseline BP.
Minimal change in BP was observed in the lower quartile (-3 ± 20 mmHg) while marked changes were observed in those with the highest quartile of baseline blood pressure (-35 ± 25 mmHg). Seventeen patients experienced an adverse event, including hypotension in 11/17 (64%).

Conclusions: Intravenous hydralazine is a commonly prescribed agent for non-urgent cases of hypertension in the hospitalized patient. Changes in systolic BP, while related to baseline BP values, are nevertheless, highly unpredictable. These data suggest that this agent should not be used in the most hypertensive patients in the hospital setting.

Blood Pressure Reductions by Quartile

Inter-Quartile Baseline SBP Range (mmHg)	Change in SBP	p-values between quartiles
1. ≤164 (n = 49, 24.4%)	-2.6 ± 20.0	
2. 165–179 (n = 48, 23.9%)	-24.9 ± 24.2	$P < 0.0001$ vs 1
3. 180–189 (n = 48, 23.9%)	-30.9 ± 10.5	$P < 0.0001$ vs 1
4.≥190 (n = 56, 27.9%)	-35.4 ± 24.9	$P < 0.0001$ vs 1, p = 0.03 vs 2

Keywords: Hypertensive emergency; Hydralazine; Intravenous; Drug utilization

PO-139

LONG-TERM EFFICACY AND SAFETY OF COMBINATION OLMESARTAN MEDOXOMIL (OM)/AMLODIPINE BESYLATE (AML)+HYDROCHLOROTHIAZIDE (HCTZ) IN STUDY PARTICIPANTS WITH HYPERTENSION BASED ON AGE: THE TRINITY STUDY

Steven G. Chrysant†,[1] Dean J. Kereiakes,[2] Suzanne Oparil,[3] Joseph Izzo,[4] Thomas Littlejohn,[5] Michael Melino,[6] James Lee,[6] Victor Fernandez,[6] Reinilde Heyrman[6]. [1]Oklahoma Cardiovascular and Hypertension Center and University of Oklahoma College of Medicine; [2]The Christ Hospital Heart and Vascular Center and The Carl and Edyth Lindner Center for Research and Education at the Christ Hospital; [3]University of Alabama at Birmingham; [4]State University of New York at Buffalo; [5]Piedmont Medical Research Associates and [6]Daiichi Sankyo, Inc.

In a prespecified subgroup analysis of the TRINITY study, the long-term efficacy and safety of OM/AML+HCTZ were

evaluated in study participants (pts) <65 y (80.4%) and ≥65 y (19.6%). After completing the 12-wk double-blind TRINITY study, pts were administered OM 40/AML 5 + HCTZ 12.5 mg in a 40-wk open-label (OL) extension. Pts not achieving BP goal (<140/90 or <130/80 mmHg for pts with diabetes, chronic renal disease, or cardiovascular disease) after 2 weeks were randomly titrated to OM 40/AML 5 + HCTZ 25 mg or OM 40/AML 10 + HCTZ 12.5 mg. At wk 16, pts not achieving BP goal were further titrated to OM 40/AML 10 + HCTZ 25 mg. Back-titration to a lower dose of triple therapy was allowed at the investigator's discretion. Study objectives were SeDBP and SeSBP at each OL visit (weeks 12–52), percentage (%) of pts reaching BP goal, and safety assessments. At wk 12 (OL start), mean BP (on treatment) was 134.2/83.3 mmHg (<65 y) and 137.5/78.0 mmHg (≥65 y). At wk 52/early termination (ET), mean SeDBP ranged from 78.5 to 83.8 mmHg (<65 y) and from 74.0 to 77.5 mmHg (≥65 y); mean SeSBP ranged from 124.7 to 136.6 mmHg (<65 y) and from 126.2 to 137.8 mmHg (≥65 y). The % of pts reaching BP goal ranged from 45.0% to 79.8% (<65 y) and from 42.3% to 79.9% (≥65 y). Most AEs were mild or moderate in severity. In pts <65 y and ≥65 y, the incidence of AEs was 36.0–58.7% and 37.2–60.9% and the incidence of drug-related AEs was 9.9–19.4% and 13.3–21.1%, respectively. Long-term treatment with OM/AML+HCTZ in pts <65 y and ≥65 y was well-tolerated (there was no distinctive AE profile for either age group) and the proposed titration scheme was effective.

Keywords: Olmesartan; Amlodipine; Hydrochlorothiazide; Age

PO-140

LONG-TERM EFFICACY AND SAFETY OF COMBINATION OLMESARTAN MEDOXOMIL (OM)/AMLODIPINE BESYLATE (AML)+HYDROCHLOROTHIAZIDE (HCTZ) — THE TRINITY STUDY: A SUBGROUP ANALYSIS BY STUDY PARTICIPANT RACE

Steven G. Chrysant†,[1] Dean J. Kereiakes,[2] Joseph Izzo,[3] Thomas Littlejohn,[4] Suzanne Oparil,[5] Michael Melino,[6] James Lee,[6] Victor Fernandez,[6] Reinilde Heyrman[6]. [1]Oklahoma Cardiovascular and Hypertension Center and University of Oklahoma College of Medicine; [2]The Christ Hospital Heart and Vascular Center and The Carl and Edyth Lindner Center for Research and Education at the Christ Hospital; [3]State University of New York at Buffalo; [4]Piedmont Medical Research Associates; [5]University of Alabama at Birmingham and [6]Daiichi Sankyo, Inc.

The long-term efficacy and safety of OM/AML+HCTZ were evaluated in black (B, 29.5%) and non-black (NB, 70.5%) study participants (pts) in a prespecified subgroup analysis of the TRINITY study. After completing the 12-wk double-blind TRINITY study, pts were administered OM 40/AML 5 + HCTZ 12.5 mg in a 40-wk open-label (OL) extension. Pts not achieving BP goal (<140/90 or <130/80 mmHg for pts with diabetes, chronic renal disease, or cardiovascular disease) after 2 weeks were randomly titrated to OM 40/AML 5 + HCTZ 25 mg or OM 40/AML 10 + HCTZ 12.5 mg. At wk 16, pts not achieving BP goal were further titrated to OM 40/AML 10 + HCTZ 25 mg. Back-titration to a lower dose of triple therapy was allowed at the investigator's discretion. Study objectives were SeDBP and SeSBP at each OL visit (weeks 12–52), percentage (%) of pts reaching BP goal, and safety assessments. At wk 12 (OL start), mean BP (on treatment) was 135.7/84.0 mmHg (B) and 134.5/81.6 mmHg (NB). At wk 52/early termination (ET), mean SeDBP ranged from 79.5 to 83.5 mmHg (B) and from 77.2 to 82.0 mmHg (NB); mean SeSBP ranged from 125.6 to 136.2 mmHg (B) and from 124.8 to 137.1 mmHg (NB). The % of pts reaching goal ranged from 47.3% to 74.6% (B) and from 42.9% to 81.4% (NB). In B and NB pts, the incidence of AEs was 30.2–56.6% and 39.3–60.5% and the incidence of drug-related AEs was 5.4–16.8% and 12.8–21.3%, respectively. Most AEs were mild or moderate in severity. Long-term treatment with OM/AML+HCTZ was well tolerated and the proposed titration scheme was effective in both race subgroups.

Keywords: Olmesartan; Amlodipine; Hydrochlorothiazide; Black

PO-141

COMPARISON OF VALSARTAN/AMLODIPINE ADDED TO DIURETIC WITH LOSARTAN ADDED TO DIURETIC ON BP LOAD IN HYPERTENSION

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Background: Blood pressure (BP) load derived from 24-hr ambulatory BP (ABP) recording is a significant predictor for target organ damage in patients with arterial hypertension. In the management of arterial hypertension, use of single-pill combination of antihypertensive agents increases the therapeutic adherence.

Objective: We evaluated the efficacy of single-pill combination valsartan 160 mg/amlodipine 5 mg added to hydrochlorothiazide (HCTZ) 25 mg (V/A/H) compared with maximum dose losartan (100 mg) added to HCTZ 25 mg (L/H) on the BP load in patients with stage 2 hypertension.

Methods: This 6-week double-blind, parallel-group study compared 2 combination treatments in patients (mean age 56.1 ± 8.2 years) on the systolic (SBP) and diastolic blood pressure (DBP) load with stage 2 hypertension receiving (V/A/H) (n = 36, baseline office BP 150.1 ± 14.95/ 87.5 ± 12.01 mmHg) vs (L/H) (n = 48, baseline office BP 148.1 ± 13.78/ 86.1 ± 11.4 mmHg). After a 1–2 week wash-out, patients were randomized to the single-pill combination of V/A 160/5 mg daily or L 100 mg. At week 3, regimens were force-titrated to add HCTZ in both arms (V/A/H 160/5/25 mg or L/H 100/25 mg). 24 hr ABP recording was performed at baseline and after 6 weeks of treatment. SBP and DBP load were defined respectively as the percent readings of ASBP > 140 mmHg and ADBP > 90 mmHg.

Results: After 6 weeks of therapy, ASBP load decreased from 70.2 ± 25.1% at baseline to 21.7 ± 25.4% (P < 0.0001) in the V/A/H group and from 68.3 ± 30.4% to 30.8 ± 30.8% in the L/H group (P < 0.0001); with significantly greater reductions with V/A/H vs L/H (P = 0.03). ADBP load decreased from 42.6 ± 32.4% at baseline to 12.8 ± 22.3% (P < 0.0001) in the V/A/H group and from 40.0 ± 33.8% to 20.0 ± 26.9% in the L/H group (P < 0.0001). The reduction was significantly greater with V/A/H than with L/H (P = 0.03).

Conclusion: Initiating treatment with a single pill combination of valsartan/amlodipine added to HCTZ is more effective than therapy with a maximal dose of losartan with HCTZ on systolic and diastolic blood pressure load.

Keywords: Combination therapy; Stage 2 hypertension; Ambulatory blood pressure monitoring; Blood pressure load

PO-142

THE IMPACT OF INITIAL TREATMENT OF HYPERTENSION ON CONTROL IN THE FIRST YEAR: COMPARISON OF INITIAL MONOTHERAPY, FREE-DOSE COMBINATION AND FIXED-DOSE COMBINATIONS

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Background: Previous clinical efficacy studies in hypertension showed that initial therapy with single-pill combinations(SPC) achieves more rapid blood pressure(BP)control than initial monotherapy(MONO) with sequential add-on. Other studies reported better adherence to SPC than to the same medications as free-dose combinations(FREE).

Objective: Determine the effectiveness of initial therapy with MONO,FREE, or SPC in achieving BP control in previously untreated hypertensives.

Methods: Summary electronic record system data were obtained from 197 practices in the Southeast US providing care for >500,000 hypertensives. Hypertensive patients seen initially from 01/2004 – 06/2009 were included if they were uncontrolled and untreated for ≥6 mo prior to initial therapy and had ≥1 one year BP follow up data. Patients with Stage 4–5 chronic kidney disease were excluded. Control was determined by the first follow-up visit with BP <140/<90 for patients without diabetes or CKD and <130/<80 for patients with either of both conditions. A total of 107,870 patients were included.[figure1]

Results: Patients on initial SPC were 3–5 years younger and more likely to be women and have Stage 2 HTN than FREE or MONO ($P < 0.0001$). In univariable hazards regressions, initial SPC (HR 1.27, 95% CI [1.23–1.30]) was more likely to produce BP than FREE (1.03 [1.01–1.05]) which was more likely to produce control than MONO. In multivariable regression adjusting for age, sex, initial BP, site of care (VA, non-VA), diabetes and CKD, SPC(1.21 [1.18–1.25]) and FREE (1.08, [1.06–1.10]) remained predictive of BP control. Including race/ethnicity in the model for 51,860 patients with data, did not significantly alter the respective HRs (SPC 1.26 [1.22–1.30];FREE 1.08 [1.05–1.12]).

Conclusion: These findings suggest that initial SPC is clinically effective for achieving more rapid BP control, which confirms and extends results from clinical efficacy studies.

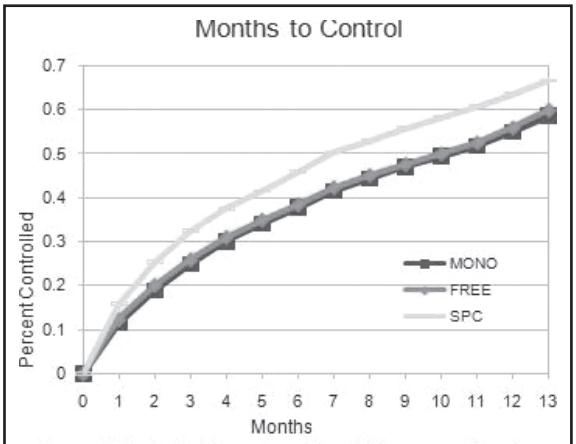

Figure 1. Univariable and multivariable proportional hazards regression was used to assess the relationship of initial treatment to BP control.
'0' Months denotes initiation of SPC, FREE or MONO.

Keywords: Hypertension; Monotherapy; Free-dose combination; Fixed-dose combination

PO-143

A BEDTIME DOSE OF ARB REDUCES URINARY ALBUMIN EXCRETION VIA THE IMPROVEMENT OF BAROREFLEX SENSITIVITY – THE J-TOP STUDY

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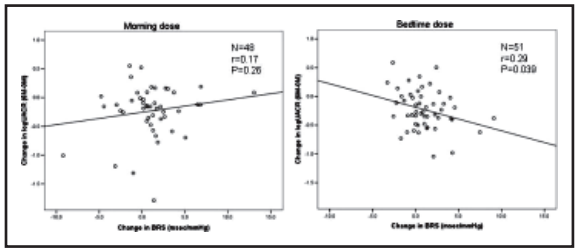
A bedtime dose of angiotensin receptor blocker (ARB) is more useful than the morning dose to reduce urinary albumin/creatinine ratio (UACR). However, the mechanism of is not well understood. We aimed this study to test the hypothesis that the improvement of baroreflex sensitivity (BRS) is the mechanism of it. This is a substudy of the J-TOP study which restricted those patients who have BRS data ($N = 109$). Subjects with morning hypertension were randomly allocated to receive bedtime dose or morning dose of candesartan to achieve target BP. BRS was significantly increased in the bedtime dose group ($P = 0.004$), but was marginal in the morning dose group ($P = 0.05$). The differential relationships were observed in the relationship between the change in BRS and UACR in the groups.[figure1]In conclusion, the improvement of BRS could be one of the mechanisms of urinary protection by the bedtime dose of ARB.



Keywords: Baroreflex sensitivity; Bedtime dose; Candesartan; Urinary albumin/creatinine ratio

PO-144

RESPONSE TO ALISKIREN IN PATIENTS WITH NON-CONTROLLED BLOOD PRESSURE SEEMS TO BE IRRESPECTIVE OF PREVIOUS THERAPY AND PLASMA RENIN ACTIVITY

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A link between high levels of plasma renin activity and adverse outcomes, including mortality, has newly focused the attention on the study of RAS (Renin-Aldosterone-System).

Aims: To evaluate if the addition of aliskiren to any antihypertensive therapy may achieve a significant and safe reduction in SBP, DBP, PP and MAP. To study if the response to aliskiren is influenced by baseline PRA levels.

Material & methods: *N* = 16, 62.9 (10.8) years, 70% males, 75% hyperglycemics, 56% MS. All of them with blood pressure above goals (ESH-2009 guidelines). Previous therapy (number of antihypertensive drugs): 1 (*n* = 4); 2 (n = 8); at least 3: (*n* = 6) Aliskiren (ALK) dosage: starting dose of 150 mg, up to 300 mg. Average follow-up: 8 months. Primary hypertension: defined according to international criteria (JNC7/ESH09). Blood pressure (OMRON 705 CP): systolic and diastolic blood pressures (SBP and DBP) and heart rate (HR). Pulse Pressure PP=SBP-DBP). Mean Arterial Pressure (MAP): DBP + 1/3 PP. Anthropometric parameters: weight (kg), body mass index (BMI) (kg/m2) and waist circumference (centimeters). Complete Blood Count: GEN-S Coulter. Biochemical parameters [glucose, creatinine, triglycerides, total cholesterol, HDL, LDL (mg/dl)]: HITACHI autoanalyzer. Statistical analysis: Mean (SD). Kolmogorov–Smirnov test. Student-t test or Mann–Whitney-U test as appropriate. Pearson's correlation coefficient.

Results: 1-Blood pressure decreased after ALK treatment: SBP p = 0.001; DBP (NS); MAP: *P* = 0. 004; PP: *P* = 0.007. 2-No significant changes were observed neither in HR nor plasma potassium. 3-No linear correlation was found between baseline PRA and changes in SBP or DBP.

Conclusions: 1-Aliskiren reduces more the systolic than the diastolic blood pressure. The MAP and PP drop significantly. 2- This new drug behaves as a safe and effective drug in the management of patients with blood pressure above the standard goals regardless of previous therapy and PRA levels.

Keywords: Aliskiren; Renin-aldosterone-system; Blood pressure

PO-145

IMPACT OF INITIAL COMBINATION THERAPY VS MONOTHERAPY ON MAJOR CARDIOVASCULAR (CV) EVENTS: A MATCHED COHORT STUDY

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Although it is generally recognized that combination therapy is required in most hypertensive patients to achieve target BP, the impact of initiating combination treatment vs monotherapy on the frequency of major CV events has not been determined. This study evaluated the real-world impact on CV event rates of initiating antihypertensive treatment with a drug combination (single-pill combination [SPC] or dual free combination) vs initiating monotherapy and switching to an SPC or adding a second agent at the discretion of the treating physician. Electronic medical records from a large integrated health delivery system were analyzed for the period between 01/2005 and 11/2009. Adult patients with uncontrolled BP initiating combination treatment were matched 1:1 with monotherapy patients later switched to a SPC or free combination (switcher/add-on) based on exact matching factors and propensity scores. Combination and monotherapy cohorts (2432 subjects in each group), were well-matched with respect to age (mean 63 yrs), gender (54% female), baseline BP (mean 149/83 mmHg), BP stage (stage 2- 30%), concomitant medications, co-morbidities, and healthcare resource use at baseline. Conditional Poisson models accounting for matched pairs were used to compare the rate of incident CV events between matched cohorts based on a composite endpoint of MI, stroke, hospitalization for heart failure, and death. Initiating treatment on combination therapy was associated with better BP control during treatment follow-up compared to patients initiating monotherapy. The risk of developing a CV event was significantly lower for the combination therapy group compared to the switcher/add-on group (Table; IRR = 0.67, 95% CI =0.53–0.84, *P* = 0.0005).

Results stratified by type of major CV event were similar. In this real-world matched-cohort study, initiating treatment on combination therapy was associated with a lower risk of developing a major CV event compared to patients switching to combination therapy.

Frequency and Incidence Rate of CV Events

Study cohort	Mean follow-up time (in days)	Frequency of CV events	Incidence rate (per 100 patients-year)
Combination	975 ± 529	190	4.25
Switcher/Add-On	1114 ± 445	251	5.12

Keywords: Hypertension; Single-pill combination therapy; Cardiovascular event

PO-146

RELATIONSHIP BETWEEN SLEEP-TIME BLOOD PRESSURE CONTROL AND REDUCTION OF URINARY ALBUMIN EXCRETION AFTER TIMED-TREATMENT WITH OLMESARTAN IN ESSENTIAL HYPERTENSION

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Clinical studies have indicated that administration of angiotensin-receptor blockers (ARB) at bedtime as opposed to upon awakening increases their efficacy in lowering sleep-time blood pressure (BP) without any loss in reducing awake BP mean. Urinary albumin excretion (UAE) in non-dippers, as well as in patients with nocturnal hypertension, has been shown to be significantly greater than in dippers, although the potential effects on renal function of specifically reducing sleep-time BP have not been clearly elucidated. Accordingly, we evaluated the administration-time-dependent effects on ambulatory BP and UAE of the ARB olmesartan in subjects with essential hypertension. We studied 203 previously untreated non-proteinuric hypetensive subjects (58 men), 48.5 ± 13.3 years of age, assigned to receive olmesartan

(40 mg/day) in monotherapy either upon awakening or at bedtime. BP was measured at 20-min intervals from 07:00 to 23:00 h and at 30 min intervals at night for 48 h before and after 12 weeks of treatment. The subjects collected their urine during the first 24 h of each BP monitoring session. The BP reduction during diurnal activity was similar for both treatment-times ($P > 0.623$). Treatment at bedtime, however, was significantly more efficient in reducing sleep-time BP (16.4/12.0 mmHg reduction in systolic/diastolic BP vs 11.6/8.3 mmHg after treatment on awakening; $P < 0.001$). The sleep-time relative BP decline was significantly increased towards a more dipping pattern only after bedtime dosing ($P < 0.001$). UAE was significantly reduced after treatment, and to a significant larger extent after bedtime dosing ($P < 0.001$). This UAE reduction was independent of the change in awake BP mean after treatment, but highly correlated with both the decrease in sleep-time BP and the increase in sleep-time relative BP decline ($r > 0.329$; $P < 0.001$), independently of treatment-time. Bedtime administration of olmesartan provides a greater efficacy as compared to morning treatment in reducing the sleep-time BP mean. This might be clinically relevant, as nighttime BP is a better prognostic marker of cardiovascular mortality than awake BP. Most important, the reduction in sleep-time BP mean and normalization of the circadian BP pattern towards a more dipper profile are associated with a significant decrease in UAE.

Keywords: Olmesartan; Albuminuria; Chronotherapy; Sleep-time blood pressure

PO-147

NEBIVOLOL AND HYDROCHLOROTHIAZIDE IN AFRICAN-AMERICANS WITH HYPERTENSION: EFFECTS ON DIASTOLIC AND ENDOTHELIAL FUNCTION

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Background: African-Americans have a greater risk of heart failure than comparator populations of white European origin. A reason for this in African-Americans is that reduced nitric oxide bioavailability results in an increased prevalence of factors that contribute to ventricular dysfunction. We wished to determine the effects of nebivolol in conjunction with hydrochlorothiazide (HCTZ) in African-American patients with hypertension and diastolic dysfunction.

Methods: 42 African-American patients with Stage I or II hypertension (systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg), a left ventricular ejection fraction $>$0.50, and echocardiographic evidence of diastolic dysfunction were assigned to nebivolol and HCTZ in an open label fashion for 24 weeks. Changes in blood pressure (BP) and success in attaining target BP were determined. Echocardiography, including tissue Doppler imaging (TDI), was measured. As a determinant of endothelial function, serum asymmetric dimethyl arginine (ADMA) levels were performed at baseline and after the treatment period.

Results: The systolic BP decreased from 150 ± 13 to 136 ± 16 mmHg ($p < 0.005$) following the 24 week treatment period. Diastolic BP decreased from 94 ± 13 to 84 ± 9 mm Hg ($P = 0.008$) in the same time period. Of the patients that completed the study, 77% achieved a combined target BP of systolic BP$<$140 mm Hg and and diastolic BP$<$90 mm Hg. ADMA levels decreased by 44% following treatment with nebivolol for 24 weeks. The change in systolic BP was strongly correlated to the change in ADMA ($r = 0.54$; $P = 0.024$). Furthermore, in comparison to a group of age-matched African-American hypertensive patients controlled with diuretic therapy only, ADMA levels were significantly lower in the nebivolol post-treatment group (controlled BP with diuretic: 0.32 ± 0.07; nebivolol post-treatment: 0.24 ± 0.06 μmol/l, $P < 0.05$).

Conclusion: Reduction in blood pressure with nebivolol in African-American patients with hypertension is correlated with improved endothelial function. Furthermore, in comparison to patients with controlled BP on diuretic therapy only, this improvement in endothelial function and increased nitric oxide bioavailability appears to be related to nebivolol therapy and suggests a potential mechanism of its efficacy.

Keywords: Endothelium; Ethnic; Nitric oxide; Diastolic function

PO-148

PERIPHERAL EDEMA ASSOCIATED WITH CALCIUM ANTAGONISTS

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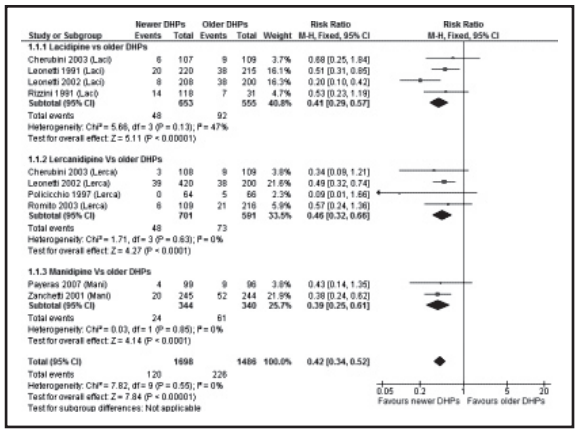
Introduction: Dihydropyridine (DHP) calcium antagonists are widely used for the treatment of hypertension. The antihypertensive effect is due to peripheral arteriolar vasodilatation. Peripheral edema is a common, dose dependent adverse effect of this class of drugs and often the reason for withdrawal thought to be due this vasodilatory effect. Newer lipophilic dihydropyridines (lacidipine, lercanidipine and manidipine) have been associated with lesser adverse effects due to their lipophilicity. We aimed to compare both the incidence and patient withdrawal due to edema with older DHPs (amlodipine, nifedipine) with newer lipophilic DHPs.

Methods: We performed a MEDLINE/CENTRAL/COCHRANE search for all the prospective randomized controlled trials in patients with hypertension, comparing lipophilic DHPs with older DHPs from 1990 to present. Trials reporting the incidence of peripheral edema or withdrawal of patients due to edema and total sample size more than 100 were included in this analysis. Incidence of edema was based on inverse variance weighted mean method. Effect estimates were pooled across studies using fixed-effects meta-analysis and heterogeneity was assessed using the I2 statistics.

Results: 8 trials with the total of 2910 patients (mean age 63 years, 58% males) and the mean follow up of 29 weeks fulfilled the criteria and were included in the analysis. 120 of 1698 patients (6.2%) developed peripheral edema on lipophilic DHPs compared to 226 of 1486 patients (13.5%) on older DHPs. The risk of peripheral edema with lipophilic DHPs was 58% lower than older DHPs (RR 0.42; 95% CI, 0.34–0.52). Similarly the risk of withdrawal due to edema was 79% lower with lipophilic DHPs compared to older DHPs (RR 0.21; 95% CI, 0.12–0.39). All lipophilic DHPs were similar in efficacy in reducing edema rates.[figure1]

Conclusion: In patients with hypertension, lipophilic DHPs had a significantly better adverse effect profile with respect to both incidence and patient withdrawal due to peripheral edema.



Keywords: Calcium antagonists; Peripheral edema

PO-149

EFFICACY OF A SIMPLIFIED MECHANISTIC ALGORITHM FOR MANAGEMENT OF RESISTANT HYPERTENSION: A RETROSPECTIVE STUDY

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This retrospective chart review assessed the clinical efficacy of a recently-described, simplified, mechanism-based algorithm for managing resistant hypertension (RH) (J Clin Hypertens, in press). The records of consecutive new patients with RH, seen by the investigator (SM), were reviewed. 34 patients met criteria of RH, of whom 8 were lost to follow-up after ≤2 visits, leaving 26.

Assuming treatment at entry included a diuretic and a drug directed at the renin-angiotensin system (ACEI, ARB, DRI or β–blocker), algorithm-based intervention consisted of either or both of 2 options, with initial choice based on clinical suspicion of volume (Option A) vs neurogenic (Option B) origin of RH:

Option A:

strengthen the diuretic regimen, usually by addition of a K^+-sparing agent

Option B:α -blocker + non-metabolized β-blocker (if needed to assure bioavailability)

BP was controlled in 24/26 patients, including 19/20 with entry SBP <160, and 5/6 with entry SBP ≥160. BP was controlled by Option A in 9 (35%), Option B in 6 (23%), and both Option A&B in 5 (19%), and, in 3, BP normalized before any intervention. Number of BP drugs increased slightly from 3.9 to 4.3.

Algorithim-based treatment utilizing Option A (strengthened diuretic regimen) and/or Option B (α -blocker + non-metabolized β-blocker regimen), without the need for additional interventions, controlled RH in 88.5% of cases. Strikingly, the 2 agents most frequently added, a K^+-sparing diuretic and an α-blocker, were clearly the least used drugs at entry. Switching to a non-metabolized β–blocker (betaxolol, bisopolol, or pindolol) or one whose metabolite is active (nebivolol), may also be important. The algorithm has the potential to both simplify and improve the management of RH and merits investigation in prospective studies.

Table I.

Drugs employed pre- and post-intervention

Drug Class	Pre-	Post-	Drug Class	Pre-	Post-
Thiazide or Loop Diuretic	24	24	All ß-blockers	21	19
K-sparing Diuretic	3	16	(a) Metab ß-Blockers	15	6
CCB	11	9	(b) *Non-metab ß-Blockers	7	14
ACEI, ARB or DRI	23	22	*α-Blocker	7	15
Vasodilator	4	1	*α- + non-metab ß-Blocker	1	10
Central α-agonist	5	4			

*Excludes labetalol, carvedilol and metoprolol whose bioavailability is unreliable due to first pass hepatic metabolism.

Keywords: Resistant hypertension; Beta-blockers; Spironolactone; Alpha-blockers

PO-150

LONG-TERM EFFICACY AND SAFETY OF COMBINATION OLMESARTAN MEDOXOMIL (OM)/AMLODIPINE BESYLATE (AML)+HYDROCHLOROTHIAZIDE (HCTZ) — THE TRINITY STUDY: SUBGROUP ANALYSES BASED ON STUDY PARTICIPANT DIABETES STATUS AND BMI

Suzanne Oparil†,[1] Joseph Izzo,[2] Steven G. Chrysant,[3] Dean J. Kereiakes,[4] Thomas Littlejohn,[5] Michael Melino,[6] James Lee,[6] Victor Fernandez,[6] Reinilde Heyrman[6]. [1]University of Alabama at Birmingham; [2]State University of New York at Buffalo; [3]Oklahoma Cardiovascular and Hypertension Center & University of Oklahoma College of Medicine; [4]The Christ Hospital Heart and Vascular Center & The Carl and Edyth Lindner Center for Research and Education; [5]Piedmont Medical Research Associates and [6]Daiichi Sankyo, Inc.

In prespecified subgroup analyses, the long-term efficacy and safety of OM/AML+HCTZ were evaluated by diabetes status (diabetes mellitus [DM;15.8%] or non-DM [84.2%]) and BMI (<30 kg/m^2 [36.9%] or ≥30 kg/m^2 [63.1%]). After completing the 12-wk double-blind TRINITY study, study participants (pts) were administered OM 40/AML 5 + HCTZ 12.5 mg in a 40-wk open-label (OL) extension. Those not achieving BP goal (<140/90 or <130/80 mmHg for pts with diabetes, chronic renal disease, or cardiovascular disease) after 2 weeks were randomly titrated to OM 40/AML 5 + HCTZ 25 mg or OM 40/AML 10 + HCTZ 12.5 mg. At wk 16, those not achieving BP goals were further titrated to OM 40/AML 10 + HCTZ 25 mg. Back-titration to a lower dose of triple therapy was allowed at the investigator's discretion. The study objectives were SeBP at each OL visit (weeks 12–52), percentage (%) of pts reaching BP goal, and safety assessments. Mean BP (mmHg; on treatment) at wk 12 (OL start):138.9/81.2 (DM);134.1/82.5 (non-DM);133.3/80.7 (BMI <30); and 135.7/83.2 (BMI ≥30). At wk 52/early termination (ET), mean SeDBP ranged from 74.9 to 79.7 mmHg (DM) and from 78.0 to 83.5 mmHg (non-DM); mean SeSBP ranged from 121.4 to 136.7 mmHg (DM) and from 125.2 to 136.8 mmHg (non-DM). At wk 52/ET, mean SeDBP ranged from 76.2 to 81.2 mmHg (BMI <30) and from 78.3 to 83.1 mmHg (BMI ≥30); mean SeSBP ranged from 124.9 to 135.9 mmHg (BMI <30) and from 125.0 to 137.2 mmHg (BMI ≥30).The % of pts reaching BP goal ranged from 24.4% to 64.5% (DM), 51.6% to 81.0% (non-DM), 46.5% to 79.2% (BMI <30), and from 43.7% to 80.3% (BMI ≥30) at

wk 52/ET. Most drug-related AEs were mild or moderate and not different between subgroups. We conclude that long-term treatment with OM/AML+HCTZ is effective and well tolerated regardless of diabetes status or body weight.

Keywords: Olmesartan; Amlodipine; Diabetes; Obesity

PO-151

WITHDRAWN AT AUTHORS' REQUEST

PO-152

DIFFERENTIAL CARDIOPROTECTIVE EFFECTS OF CARVEDILOL AND VALSARTAN UNDER DIFFERENT CARDIAC LOADING CONDITIONS

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Background: Although the combination of ACE inhibitor (ACE I) and beta-blocker is recommended for ischemic heart disease, whether this combination is hemodynamically advantageous in hypertension is not known. The present study was performed to determine whether the cardioprotective effect of carvedilol (C) as compared to angiotensin receptor blocker (ARB) are affected by different levels of cardiac load when added to background ACE I therapy.

Methods: The study included 30 hypertensive subjects with a 3-week run-in period of lisinopril monotherapy (40 mg/day) after which each subject received C (20 then 40 mg/day) or valsartan (V, 160 then 320 mg/day) for 4 weeks each in a random-order cross-over design. At the end of each period, subjects had recumbent bicycle exercise testing at 30 and 60 watts for 3 min each. Daytime (6AM to midnight) and night-time BP and heart rate values were determined from 24-hr ambulatory blood pressure monitoring (Spacelabs).

Results: Primary results after each drug phase are shown in Table I.

Baseline clinic values [mean (SD)] were: systolic BP [SBP, 150(18) mmHg], heart rate [HR, 71.7(13) beats/min]. The double product (SBP x HR, a common indicator of cardiac load) was 10720(2411) units at rest, 16954(4481) at 30 watts, and 19135(5930) at 60 watts. Baseline night and daytime SBP x HR were 8933(2494) and 11858(2412) units, respectively.

Conclusion: The addition of either C or V to background ACE I reduces daytime cardiac work but neither C nor V limits the increase in cardiac load during moderate exercise. Only during conditions of low cardiac load (at night or during supine rest) is C is more effective than V in reducing heart rate or cardiac work. These findings suggest that there are variable cardioprotective effects of C or V at different levels of cardiac load and that C does not block the cardiac response to low-level exercise.

	Rest	30 Watts	60 Watts	Night	Day
Valsartan (V)					
HR	75.3 (16.8)	107 (26.8)	112.6 (23.7)	71.6 (13.8)	80 (15.4)
SBP	143 (23.5)	152 (25)	162.7 (33)	126 (18.4)	134 (20)††
SBP x HR	10857.5 (3534)	16451 (5499)	18319 (5674)	9014 (2344)	10722 (3184)††
Carvedilol (C)					
HR	68 (13.7) **††	107.3 (31.6)	116 (36.3)	66 (11.6)**†	76 (15)††
SBP	146.8 (26)	159 (31)	161.1 (32.9)	127 (19)	138 (19)††
SBP x HR	9933 (2554) *†	17540 (7530)	19130 (8316)	8394 (1953)**	10362 (2426)††

*$P \leq 0.05$, **≤ 0.01, V compared to C. †≤ 0.05, ††≤ 0.01 C or V compared to baseline.

Keywords: Beta-blocker; ARB; Hemodynamics; Cardiac work load

PO-153

EFFECTS OF TIME OF HYPERTENSION TREATMENT ON THE CIRCADIAN BLOOD PRESSURE PATTERN OF SUBJECTS WITH RESISTANT HYPERTENSION: THE HYGIA PROJECT

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Subjects with resistant hypertension present high prevalence of a non-dipper blood pressure (BP) pattern, associated with increased risk of cardiovascular events. Non-dipping is partly related to the absence of 24h therapeutic coverage in hypertensives treated with single morning doses. It has been reported that as much as 89% of treated hypertensive subjects, including those with resistant hypertension, ingest all their BP-lowering medication in the morning. Accordingly, we investigated the impact of the time of day of hypertension treatment on the circadian BP pattern in subjects with resistant hypertension participating in the Hygia Project, designed to evaluate prospectively cardiovascular risk by ambulatory BP monitoring (ABPM) in primary care centers of Northwest Spain. We studied 1543 subjects with resistant hypertension (899 men/644 women), 66.8 ± 11.2 years of age. At the time of ABPM evaluation, 293 subjects were ingesting all their medication upon awakening, and the remaining subjects were taken at least one BP-lowering medication at bedtime. BP was measured by ABPM for 48h. Among subjects ingesting all BP-lowering medication upon awakening, the prevalence of extreme-dipper, dipper, non-dipper and riser BP patterns were 3.0, 26.3, 49.5 and 21.2%, respectively. The prevalence of an sleep-time relative systolic BP decline <10% (non-dippers/risers) was significantly lower with increasing number of medications ingested at bedtime, and it was at a minimum 46% prevalence when subjects were ingesting all BP-lowering medication at bedtime ($P < 0.001$). Increased number of medications at bedtime was also associated with a progressive improved control on nighttime BP. In subjects with resistant hypertension, pharmacological therapy should take into account when to treat with respect to the rest-activity cycle of each individual patient. Treatment at bedtime is characterized by increased nighttime BP control and a significantly lower prevalence of a non-dipper and mainly riser BP pattern, therapeutic targets that have already been shown to significantly reduce cardiovascular risk.

Keywords: Chronotherapy; Resistant hypertension; Ambulatory blood pressure

PO-154

PLASMA RENIN-GUIDED TREATMENT IN YOUNG UNTREATED HYPERTENSION: A RANDOMIZED COMPARATIVE PILOT STUDY

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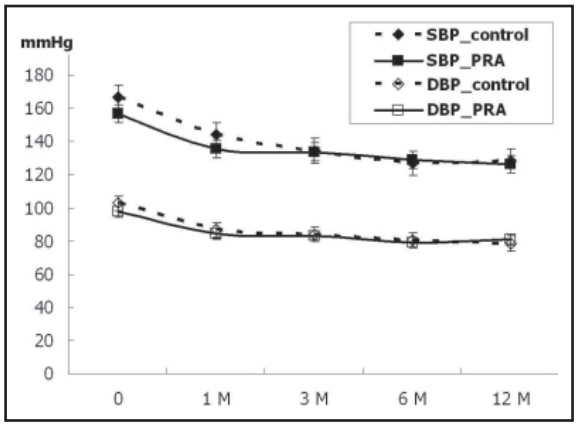
Renin-guided therapeutics using plasma renin activity (PRA) values may lead to clinically significant blood pressure (BP) reductions. We were to compare the effect of renin-guided therapy vs (not renin-based) routine practice on short-term BP reductions in young untreated hypertensive patients who mostly have high renin activity would benefit from renin-targeted antihypertensive drugs.

Thirty-two young untreated hypertensive patients less than 55 years old were randomized to either renin-guided group (PRA group, $n = 16$) or routine practice (Control group, $n = 16$) managed by different specialists in hypertension clinic. After the blood samples for PRA were drawn at the first visit, randomization was made after one week. PRA group received antihypertensive drug based on their PRA, i.e. either angiotensin converting enzyme inhibitor or angiotensin receptor blocker if their PRA ≥0.65 ng/ml/h, calcium antagonist or diuretics if PRA< 0.65 ng/ml/h. Control group received antihypertensive drug selected by a specialist blinded to PRA value. If the BP has not reached the goal (<140/90mmHg) after 2 months, both group received another class of antihypertensive drugs added.

The study subjects were 45 years old in average (from 33 to 54). PRA group had similar initial BP (systolic BP, 156.8 ± 14.5 vs 166.9 ± 18.2 mmHg; diastolic BP, 97.7 ± 10.7 vs 102.9 ± 12.3 mmHg) and showed similar BP reduction after one year study period (systolic BP, 126.2 ± 9.4 vs 128.0 ± 10.5 mmHg; diastolic BP, 80.8 ± 6.1 vs 78.4 ± 7.2 mmHg) compared to Control group. In conclusion, plasma renin-guided treatment in young untreated hypertension does not seem to be more effective for the short-term BP reduction than the routine practice independent of PRA value.[figure1]



Keywords: Plasma renin activity; Antihypertensive drug

PO-155

ANGIOTENSIN CONVERTING ENZYME INHIBITORS OR ANGIOTENSIN RECEPTOR BLOCKERS AS FIRST-LINE TREATMENT IN PATIENTS WITH UNCOMPLICATED HYPERTENSION?

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The aim of this cross-sectional study was to compare the effects of angiotensin converting enzyme inhibitors (ACE-I) and angiotensin

receptor blockers (ARB) in patients with uncomplicated hypertension. The medical notes of the most recent visit to our Outpatient Clinic of 1,810 hypertensive patients (40.4% males, age 56.5 ± 13.5 years) were analyzed. Of them, 32.0% were receiving ACE-I (alone or in combination with other antihypertensive agents), 10.5% were receiving ARB (alone or in combination with other antihypertensive agents), 57.2% were not receiving either of these agents, and only 0.3% were receiving both classes. Patients who were on ARB were more frequently smokers and had a higher prevalence of the metabolic syndrome compared with patients who were on ACE-I (smoking: 31.6 and 22.8%, respectively, $P < 0.05$; metabolic syndrome: 28.4 and 18.5%, respectively, $P < 0.005$). Despite these adverse characteristics, patients who were receiving ARB had lower systolic blood pressure (144 ± 23 vs 151 ± 23mmHg, $P < 0.001$), diastolic blood pressure (83 ± 14 vs 91 ± 13mmHg, $P < 0.001$) and serum triglyceride levels (1.5 ± 0.7 vs 1.8 ± 0.9 mmol/l, $P < 0.001$) compared with patients who were receiving ACE-I alone or in combination with other antihypertensive agents. Patients who were on ARB were more frequently on blood pressure target compared with patients on ACE-I (28.8 and 15.7% respectively, $p < 0.001$). Serum potassium levels were higher in patients who were receiving ARB than in those on ACE (4.4 ± 0.5 and 4.2 ± 0.4 mmol/l, respectively, $P < 0.001$) but the estimated glomerular filtration rate (assessed with the Modification of Diet in Renal Disease equation) did not differ between the 2 groups (76.3 ± 23.7 vs 79.9 ± 19.7 ml/min/1.73m^2, respectively; $P = 0.160$). When patients who were on monotherapy with ACE ($n = 168$) or ARB ($n = 50$) were analyzed separately, similar differences between the 2 groups were observed. In conclusion, ARB appear to be more effective on blood pressure lowering and have a more beneficial effect on serum triglyceride levels in patients with uncomplicated hypertension in a secondary-care setting.

Keywords: Angiotensin converting enzyme inhibitors; Angiotensin receptor blockers; Uncomplicated hypertension

PO-156

AMLODIPINE/VALSARTAN SINGLE PILL COMBINATION TREATMENT OF ARTERIAL HYPERTENSION IN A REAL LIFE PRACTICE IN RUSSIA

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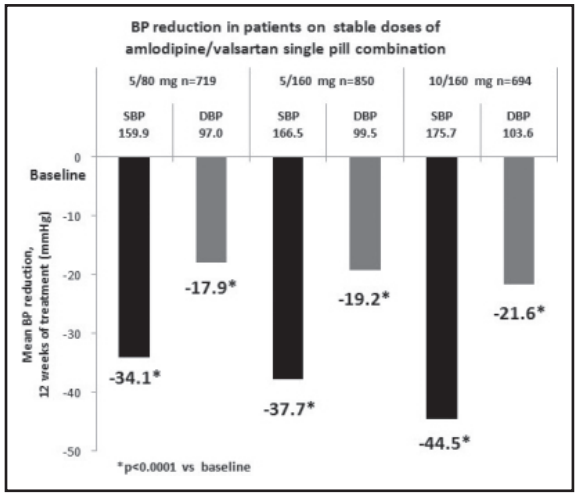
We present a sub-analysis of amlodipine/valsartan single pill combination efficacy and safety in a large subgroup of Russian Caucasian patients, which participated in a multi-centre, multinational, open-label observational non-interventional post marketing surveillance study. 2874 patients with hypertension were enrolled in Russia, 50 patients did not complete the study as per protocol (16 patients withdrew consent, 15 discontinued due to adverse events, 13 lost to follow-up, 5 discontinued due to lack of efficacy and in 1 patient medical condition no longer required study medication) and 2824 patients data was analyzed: mean age 55.7 years, 46.8% men, 24.9% smokers, 38.7% had coronary heart disease, 19.8% had heart failure, 18.8% diabetic, 89.7% received hypertension treatment before they were prescribed amlodipine/valsartan combination and enrolled in our study (69% ACE inhibitors, 49% diuretics, 43% beta-blockers, 33% calcium antagonists). The baseline SBP/DBP (167.5/100.1 mmHg) was reduced by 38.9/19.6 mmHg ($p < 0.0001$) during 12 weeks of treatment. 80% of patients reached BP goal <140/90 mmHg. Only 577 (20.4%) patients received beta-blockers and 331 (11.7%) diuretics concomitantly. We analyzed data for patients on stable doses of amlodipine/valsartan combination throughout the study period and observed dose-dependant BP reductions. BP reduction was smallest in patients with grade I hypertension and greatest in grade III patients.[figure1]

Our results show excellent BP reduction and BP control rate achieved with amlodipine/valsartan single pill combination in a real life setting in Russian Caucasian patients.

BP reduction in patients with different BP elevation at baseline

Hypertension Grade	I (SBP 140–159 mmHg)	II (SBP 160–179 mmHg)	III (SBP ≥180 mmHg)	SBP ≥190 mmHg	SBP ≥200 mmHg	SBP >140/ DBP<90 mmHg
n=	635	1449	719	296	145	122
Baseline SBP/DBP	150.0/94.9	165.2/99.4	188.9/106.3	200.5/110.1	210.7/113.5	156.4/81.3
SBP/DBP reduction	25.3/15.9	36.8/19.2	55.9/23.9	65.7/26.2	74.2/28.5	31.6/5.8
P	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001



Keywords: Hypertension; Amlodipine; Valsartan; Single pill combination

PO-157

REAL LIFE SAFETY AND EFFECTIVENESS OF AMLODIPINE/VALSARTAN SINGLE PILL COMBINATION IN THE TREATMENT OF HYPERTENSION

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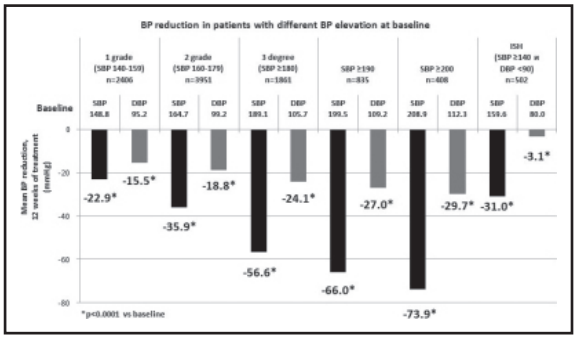
The aim of our study was to evaluate safety and effectiveness of the single pill combination of amlodipine and valsartan in patients with arterial hypertension (HTN). This was a multicenter, open-label, observational, non-interventional, post marketing surveillance study conducted in Russia, Philippines, Saudi Arabia, Middle East Countries, Thailand and India. 9090 patients with HTN were enrolled, 754 were excluded from per protocol analysis (296 were lost to follow-up, 72 discontinued due to adverse

events, 3 patients died, 348 had missing data, 35 due to other reasons). 8336 patients completed the study: mean age 54.7 years, 43.1% men, 41.3% Asian, 50.1% Caucasian, 83.4% with prior HTN treatment (discontinued), baseline blood pressure (BP) of 165.0/99.3. The significant reduction in BP (-36.3/-18.9 mmHg, $p < 0.0001$) was achieved during 12 weeks of treatment with amlodipine/valsartan single pill combination resulting in a final BP of 128.7/80.4 mmHg. We observed a dose-dependant effect with the least BP reduction for 5/80 mg dose (-32.4/-17.8 mmHg, $p < 0.0001$), average BP reduction for 5/160 mg (-34.9/18.3 mmHg) and the greatest for 10/160mg doses (-41.4/-20.6 mmHg, $p < 0.0001$). Treatment response increased with increasing severities of baseline BP with the greatest BP drops observed in grade III patients with systolic BP over 200 mmHg. The BP drops by baseline BP severity are presented. [figure1] Mean BP levels in all subgroups of patients after 12 weeks of amlodipine/valsartan single pill combination treatment were lower than 140/90 mmHg. BP control (<140/90 mmHg) was achieved in 77.7% patients at the end of the study period. Our data shows, that an optimal BP reduction was achieved for all HTN grades as well as isolated systolic HTN providing evidence that most of hypertensive patients may benefit from treatment with amlodipine/valsartan single pill combination.



Keywords: Hypertension; Amlodipine; Valsartan; Single pill combination

Clinical Trials

PO-158

THE INFLUENCE OF ANTIHYPERTENSIVE THERAPY ON BLOOD PRESSURE VARIABILITY: THE X-CELLENT STUDY

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We aimed to investigate the influence on blood pressure variability (BPV) of antihypertensive agents, and the underlying mechanisms. Among 1762 hypertensive patients from the X-CELLENT study, a randomized, double-blind, and placebo-controlled study with four parallel treatment arms (placebo, indapamide, candesartan and amlodipine), 579 subjects participated in the ambulatory blood pressure monitoring (ABPM) study. The 24-hour ABPM was performed at baseline and after a 3-month treatment. To evaluate blood pressure (BP) and its variability, within-subject 24-hour BP mean values and standard deviation (SD) were weighted by the time interval between consecutive readings, and calculated along three time frames: daytime, nighttime, all-day time. The 24-hour heart rate and heart rate variability (HRV) were calculated with the same algorithm. Although the three active drugs had a similar effect on BP reduction, only amlodipine significantly decreased SD of 4 BP components in all the time frames ($P \leq 0.038$). In subjects at baseline, the major determinants of BPV were age, mean value of 24-hour BP and corresponding HRV. Furthermore, in the amlodipine group ($n = 124$), the reduction of BPV was mainly due to the reduction of BP level and HRV, and a significant association between the reduction in BPV and in HRV was only found in the nighttime ($P \leq 0.049$). In summary, age, BP values and HRV were the major determinants of BPV. Amlodipine was the most effective antihypertensive agent in decreasing BPV, as it lowered BP values and HRV, stabilizing the autonomic nervous system, mainly at the nighttime.

Keywords: Blood pressure variability; Indapamide; Antihypertensive; Ambulatory blood pressure monitoring

PO-159

A DOUBLE-DUMMY COMPARISON OF *DE NOVO* COMBINATION VS SEQUENTIAL ADD-ON THERAPY: 'ACCELERATE'

Morris Brown,[1,2] Gordon McInnes,[1,3] Cheraz Cherif Papst,[4] Jack Zhang,[4] Thomas MacDonald[1,5]. [1]British Hypertension Society, GB; [2]University of Cambridge, GB; [3]University of Glasgow, GB; [4]Novartis Pharma AG, China and [5]University of Dundee, GB.

Delayed BP control in VALUE led to 3-fold excess mortality. Yet JNC7 advice to accelerate control by using initial combination is rarely heeded, because of concern about tolerability and unnecessary drug use. A combination is most likely to be effective and tolerated when the drugs have complementary actions on the renin system. We have tested whether maximum doses of two such drugs started together [i] achieve substantial superiority over sequential combination, with the same or better tolerability, and [ii] lead to sustained superiority by blocking neurohumoral or hemodynamic compensation.

1254 patients, SBP >150 mmHg, were randomized to *either* aliskiren (Ali) 150 mg+amlodipine (Aml) 5 mg; *or* Ali 150 mg; *or* Aml 5mg, with dose-doubling after 8 weeks. From 16–32 weeks, all patients received Ali 300 mg + Aml 10mg; HCTZ was added at 24 weeks if BP>140/90. Co-primary endpoints were the *average* reductions in SBP over 8,16 & 24 weeks, and *point* reduction at 24 weeks. LSM differences between Ali/Aml & average monotherapy were calculated by repeated measures ANCOVA. Plasma renin activity (PRA) was measured in 396 patients, and exploratory analysis conducted of BP response by baseline tertiles.

Mean baseline BP was 162/93 mmHg. The fall over 24 weeks was 6.4/3.7 mmHg greater on combination than sequential therapies ($P < 0.0001$). At 24 weeks, when all patients were on combination, the difference was 1.44 (−0.05, 2.9)/0.90(0.02, 1.8) mmHg ($P < 0.05$ for DBP). At 32 weeks, 62% of Ali/Aml were at target, vs 53% of patients started on Aml ($P = 0.02$). Only 2 patients withdrew because of hypotension, both on Aml. There were 36 withdrawals for peripheral edema from Aml (11.4%), *cf* 44 (7.1%) from Ali/Aml and 20 (6.3%) from Ali ($P = 0.035$). Ali/Aml was superior to average initial monotherapy over 24 weeks in all 3 tertiles of baseline PRA, with numerically greatest superiority in the mid-tertile of 7.99 (4.74, 11.3) mmHg *cf*. 5.11(1.56, 8.67) and 5.18(1.96, 8.40) in the low and high tertiles.

Initial combination achieved superior BP reduction to monotherapy, without excess hypotension. In patients with SBP> 150 mmHg, there appears little downside to initiating treatment

with combination, which may minimise early risk, and maximise later BP control.

Keywords: Renin; Aliskiren; Amlodipine; Combination therapy

PO-160

AMLODIPINE PLUS TELMISARTAN OR AMILORIDE FOR HYPERTENSIVE PATIENTS: FOCUS ON EFFECTS ON METABOLIC PROFILES

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Objectives: In present study was to evaluate the short-term effect of amlodipine pius telmisartan or amiloride on reduction of blood pressure in moderate and high-risk Patients. Meanwhile, we assessed the effects of these drug combinations on fasting glucose in these patients.

Methods: In this randomized, blind-end trial, 106 hypertensive patients met Inclusion criteria are enrolled. Patients were randomly assigned to amlodipine 2.5mg plus telmisartan 80mg group (AML/TEL) or amlodipine 2.5mg plus amiloride 2.5mg-hydrochlorothiazide 25mg complex(AML/AMIL- HCTZ); Amlodipine 2.5mg could be added if blood pressure beyond control at 4-week. Follow up 24 weeks. Primary efficacy parameter was reduction of blood pressure at 24-week. Physical and laboratory characteristics and side effects were recorded. Physical and laboratory characteristics and side effects were recorded.

Results: All the baseline characteristics are comparable in two groups. Both antihypertensive regimens produced statistically significant reductions from baseline in blood pressure (DSBPs 24.3 ± 15.8 vs 26.8 ± 13.4, $P > 0.05$) (DDBPs 15.2 ± 9.2 vs15.7 ± 9.4, $P > 0.05$) that were equivalent at 24-week treatment. While, the patients complicated with impaired glucose tolerance (IGTs) and diabetes mellitus (DMs) statistically differences were found between two groups in total cholesterol (3.78 ± 0.73 in AML/TEL vs 5.89 ± 1.02 in AML/AMIL- HCTZ, $P < 0.05$) and fasting glucose (6.5 ± 1.6 mmol/l in AML/TEL vs 8.8 ± 1.9mmol/l in AML/AMIL- HCTZ, $P < 0.05$). The reduction of blood pressure (DSBPs 22.4 ± 12.6 vs 24.2 ± 14.4, $p > 0.05$; DDBPs 13.5 ± 6.2 vs13.7 ± 7.4, $p > 0.05$) and adverse effects (9% vs 8.3%) were similar between two regimens in the IGTs and DMs.

Conclusion: Amlodipine-based antihypertensive combination strategies achieved satisfactory blood pressure control in hypertensive patients with moderate or high cardiovascular risk.Due to the metabolic profile was unfavourable towards the AML/AMIL-HCTZ group in the IGTs and DMs patients. Initial antihypertensive treatment with amlodipine plus telmisartan should be considered in preference to amlodipine 2.5 mg plus amiloride 2.5 mg-hydrochlorothiazide 25mg complex to control risks factors at greater extent.

Keywords: Hypertension; Impaired glucose tolerance (IGTs); Amlodipine; Diabetes mellitus (DMs)

PO-161

AMLODIPINE PLUS TELMISARTAN OR AMILORIDE FOR HYPERTENSION IN MODERATE AND HIGH-RISK PATIENTS: A 24-WEEK OBSERVATION

Jingjing Cai, Zhijun Huang, Rong Cui, Hong Yuan. The Center of Clinical Pharmacology of the Third Xiangya Hospital, Central South University, Changsha, China.

Objective: The aim of present study was to evaluate the short-term effect of amlodipine-based antihypertensive combination regimens on reduction of blood pressure and adverse effect in hypertensive patients with moderate or high risk of cardiovascular event.

Methods: In this randomized, blind-end trial, 106 hypertensive patients met Inclusion criteria are enrolled. Patients were randomly assigned to amlodipine 2.5 mg plus telmisartan 80mg group (AML/TEL) or amlodipine 2.5 mg plus amiloride 2.5 mg-hydrochlorothiazide 25mg complex(AML/AMIL- HCTZ); Amlodipine 2.5mg could be added if blood pressure beyond control at 4-week. Follow up 24 weeks. Primary efficacy parameter was reduction of blood pressure at 24-week. Physical and laboratory characteristics and side effects were recorded.

Results: Baseline systolic blood pressure was160.5 ± 16.5 mm Hg and diastolic blood pressure was 98.7 ± 9.7 mm Hg. All the baseline characteristics are comparable in two groups. After 2-week treatment, mean systolic blood pressure in AML/TEL group and AML/AMIL-HCTZ group was (151.5 ± 14.8) mm Hg and (144.4 ± 13.9) mm Hg, respectively ($P < 0.05$). Mean diastolic blood pressure in AML/TEL group and AML/AMIL-HCTZ group was reduced to (91.7 ± 9.6) mm Hg and (90.1 ± 9.4) mm Hg, respectively ($p > 0.05$). Blood pressure control rate was 47.2% and 58.1% in AML/TEL group and AML/AMIL-HCTZ group ($P < 0.05$). After 24-week therapy, there were no significant differences on reduction of blood pressures (SBPs 24.3 ± 15.8 vs 26.8 ± 13.4, $P > 0.05$) (DBPs 15.2 ± 9.2 vs15.7 ± 9.4, $P > 0.05$) or blood pressure control rates (67.9% of vs 71.7%, $p > 0.05$) in two groups. Laboratory characteristics were similar. Compared with AML/TEL group and AML/AMIL-HCTZ group, both of them reported equivalent of adverse effects (7.6% of AML/TEL vs 9.4% of AML/AMIL-HCTZ, $P > 0.05$).

Conclusion: Amlodipine-based antihypertensive combination strategies achieved satisfactory blood pressure control in hypertensive patients with moderate or high cardiovascular risk. Yet, more predominant efficacy on the reduction of blood pressure and blood pressure control rates shows in the combination of AML/AMIL-HCTZ group at 2-week follow-up. Adverse cardiovascular events and organ benefits beyond reducing blood pressure warrant longer clinical observation.

Keywords: Hypertension; Amlodipine

PO-162

EFFICACY AND SAFETY OF AZILSARTAN MEDOXOMIL/CHLORTHALIDONE VS OLMESARTAN/HCTZ COMBINATIONS IN STAGE 2 SYSTOLIC HTN

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Background: Azilsartan medoxomil (AZL-M) is a new highly potent, long-acting angiotensin II receptor blocker (ARB), and chlorthalidone (CLD) is a highly potent, long-acting thiazide-like diuretic.

Methods: We compared fixed-dose combinations (FDCs) of AZL-M/CLD 20/12.5 mg QD titrated to 40/25 mg if needed or AZL-M/CLD 40/12.5 mg QD titrated to 80/25 mg if needed and an FDC of the ARB olmesartan medoxomil (OLM) plus the thiazide diuretic hydrochlorothiazide (HCTZ) 20/12.5 mg QD titrated to 40/25 mg if needed. This was a randomized, double-blind, 8-week study of 1085 subjects with mean clinic systolic BP (SBP) 160–190 mm Hg and diastolic BP $\leq$119 mm Hg. Titration to higher doses occurred at week 4 if BP was above target. The primary endpoint was change from baseline in clinic seated trough SBP; 24-hour ambulatory BP monitoring was also conducted.

Results: Patient characteristics: mean age 56 years, 48% women, 26.7% black, 62.7% white, BMI 31.8 kg/m^2, 22.9% current smokers, and 17.3% diabetes mellitus. Changes in clinic SBP were greater with AZL-M/CLD than with OLM/HCTZ despite less titration to higher doses (Table). At 8 weeks, both AZL-M/CLD FDCs reduced 24-hour mean SBP more than OLM/HCTZ (-26.4 and -27.9 vs -20.7 mm Hg; both $p < 0.001$). Adverse events leading to temporary or permanent drug discontinuation occurred in 6.2%, 9.5%, and 3.1% of the AZL-M/CLD 40/25 mg, AZL-M/CLD 80/25 mg, and OLM/HCTZ 40/25 mg groups, respectively. No deaths occurred.

Conclusions: AZL-M/CLD FDCs reduced office and ambulatory SBP more than OLM/HCTZ in this titration-to-target study.[figure1]

Clinic	AZL-M/CLD 20/12.5→40/25 mg N=372	AZL-M/CLD 40/12.5→80/25 mg N=357	OLM/HCTZ 20/12.5→40/25 mg N=356
Baseline SBP, mm Hg	165.2±0.55	164.8±0.56	164.7±0.56
Week 4			
Change in SBP, mm Hg	-33.0±0.87	-34.1±0.88	-26.9±0.88
Difference vs OLM/HCTZ	-6.1	-7.2	
95% CI	-8.5, -3.7	-9.6, -4.8	
P vs OLM/HCTZ	<0.001	<0.001	
Subjects titrated to high dose at week 4, n (%)	143 (38.4)	124 (34.7)	184 (51.7)
Week 8			
Change in SBP, mm Hg	-37.6±0.83	-38.2±0.85	-31.5±0.84
Difference vs OLM/HCTZ	-6.1	-6.7	
95% CI	-8.4, -3.8	-9.1, -4.4	
P vs OLM/HCTZ	<0.001	<0.001	

Keywords: Hypertension; Azilsartan medoxmil; Chlorthalidone; Fixed-dose combination

PO-163

EFFECT OF ALISKIREN AND ANTIHYPERTENSIVE DRUGS ON DIASTOLIC FUNCTION IN HYPERTENSIVES WITH DIASTOLIC DYSFUNCTION: A RANDOMISED STUDY

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Background: Diastolic dysfunction might represent an important pathophysiological intermediate between hypertension and heart failure. Our aim was to determine whether the direct renin inhibitor aliskiren can improve diastolic function to a greater extent than can other antihypertensive agents.

Methods: Patients with hypertension and evidence of diastolic dysfunction were randomly assigned to receive either the direct renin inhibitor aliskiren (titrated to 300 mg once daily) or matched placebo. Patients in both groups also received concomitant antihypertensive agents that did not inhibit the renin-angiotensin system to reach targets of under 135 mm Hg systolic blood pressure and under 80 mm Hg diastolic blood pressure. The primary endpoint was change in diastolic relaxation velocity between baseline and 40 weeks as determined by tissue doppler imaging. Analyses were done by intention to treat. This study was spontaneous in according to Italian registry of drugs.

Findings: 106 patients were randomly assigned to receive aliskiren; 88 were randomly assigned to receive placebo. 18 patients were lost to follow-up or discontinued the assigned intervention. Over 40 weeks, there was a 12.8 (SD 17.2)/7.1 (9.9) mm Hg reduction in blood pressure in the aliskiren group and a 9.7 (17.0)/5.5 (10.2) mm Hg reduction in the placebo group. The difference in blood pressure reduction between the two groups was not significant. Diastolic relaxation velocity increased by 0.60 (SD 1.4) cm/s from baseline in the aliskiren group ($P < 0.0001$) and 0.44 (1.4) cm/s from baseline in the placebo group ($P < 0.0001$) by week 40. However, there was no significant difference in the change in diastolic relaxation velocity between the groups ($P = 0.29$).

Conclusion: Lowering blood pressure improves diastolic function irrespective of the type of antihypertensive agent used.

Keywords: Aliskiren; Diastolic dysfunction; Renin-angiotensin system; Diastolic relaxation velocity

PO-164

EFFECTS OF ADD-ON NEBIVOLOL ON BLOOD PRESSURE AND GLUCOSE PARAMETERS IN HYPERTENSIVE PATIENTS WITH PREDIABETES

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In this multicenter trial, the effects of nebivolol added to an ACEI or ARB on BP and glucose metabolism were assessed in patients with hypertension and prediabetes. Patients with DBP 80–110 mmHg and with impaired fasting plasma glucose (FPG: 100–125 mg/dL) and/or elevated 2-hour post-oral glucose tolerance test (OGTT: 140–199 mg/dL) at screening entered a 4-week run-in period receiving lisinopril (10 mg/day) or losartan (50 mg/day). All other antihypertensive medications were discontinued. Those with DBP 90–110 mmHg at the end of the run-in period were randomized (2:2:1) to double-blind add-on treatment with nebivolol (n = 223; 5–40 mg/day), HCTZ (n = 212; 12.5–25 mg/day), or placebo (n = 102). Double-blind treatment was titrated

to achieve SBP/DBP ≤130/80 mmHg over 12 weeks. The primary outcome measure was DBP change from baseline to week 12 (LOCF, ITT); secondary measures included changes in SBP and glucose levels. 442 patients completed the double-blind period. Baseline characteristics of treatment groups were comparable; overall mean values for BMI, TGs, and HDL cholesterol were 32.3 kg/m^2, 1.7 mmol/L, and 1.3 mmol/L, respectively. At week 12, mean trough DBP in nebivolol and placebo groups decreased by -9.4 mmHg and -5.0 mmHg, respectively ($P <$ 0.001); for SBP, those changes were -10.4 mmHg and -7.8 mmHg (P = 0.148). The mean changes in normalized AUC of OGTT in nebivolol and HCTZ groups were 0.0 mg/dL and 6.9 mg/dL (P = 0.020), compared with -1.0 mg/dL in the placebo group. A significantly smaller increase in FPG was observed with nebivolol vs HCTZ treatment (1.3 mg/dL vs 5.4 mg/dL, P = 0.002).The HOMA-IR in nebivolol and HCTZ groups increased by 0.6 and 1.5, respectively (P = 0.097; placebo: 0.0). AE-related discontinuation rates were 10.3% (nebivolol), 6.6% (HCTZ), and 2.0% (placebo); rates of serious AEs were 2.2%, 2.8%, and 2.0%, respectively. There were 4 deaths: 1 stroke and 1 cancer in nebivolol group, and 1 cardiac arrest (CA) and 1 myocardial infarction (MI) in HCTZ group; MI and cancer were considered not related, and stroke and CA were considered possibly related to study medication. These data demonstrate that nebivolol, when added to an ACEI or ARB, provided additional significant blood pressure reduction, with little or no effect on glucose metabolism, in patients with hypertension and prediabetes.

Keywords: Hypertension; Beta-blocker; Prediabetes; Nebivolol

PO-165

INCIDENT DIABETES WITH ANTIHYPERTENSIVE DRUGS: UPDATED NETWORK AND BAYESIAN META-ANALYSES OF CLINICAL TRIAL DATA

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Our 2007 network meta-analysis of the 22 existing clinical trials of antihypertensive drugs that reported data about new-onset diabetes (NOD, *Lancet*. 2007;**369**:201–207, errata 1518) was challenged because multi-arm trials may have been over-represented, and because it takes nearly a decade for NOD to increase cardiovascular risk significantly. Since then, several large trials (TRANSCEND, PRoFESS) showed a non-significant effect of an angiotensin receptor blocker (ARB), and ONTARGET concluded that an ACE-inhibitor had less NOD than did an ARB. We therefore updated our original analyses with 12 more trials (6781 more cases of NOD, 68,823 more subjects), and performed network and Bayesian meta-analyses of all existing data. The numbers of new cases of incident diabetes/number at risk (number of trials) were: Placebo 4838/51,310 (17); Diuretic 988/29,029 (9); Beta-blocker 2708/44,288 (10); Calcium channel blocker (CCB) 2893/56,400 (12); ACE-inhibitor 2329/39,830 (10); ARB 4037/46,636 (14). As previously, the method of Lumley was used for network meta-analyses; Bayesian meta-analyses were performed with WINBUGS 1.4.1, with non-informative priors, a burn of 1000, and 99,000 iterations. The incoherence value for the network meta-analysis was 0.06269. The odds ratios (and 95% confidence intervals, CI) and posterior probabilities (and 2.5–97.5% credible intervals, CrI) for the meta-analyses were:

Drug Class	Network Meta-analysis Odds Ratio (95% CI)	Bayesian Meta-analysis Posterior Probability (2.5–97.5% CI)
Diuretic	1.00 (referent)	1.00 (referent)
Beta-blocker	0.93 (0.79–1.11)	0.89 (0.77–1.02)
CCB	0.80 (0.69–0.94)	0.77 (0.68–0.88)
Placebo	0.75 (0.64–0.88)	0.75 (0.65–0.85)
ACE-inhibitor	0.66 (0.56–0.77)	0.65 (0.57–0.74)
ARB	0.64 (0.54–0.76)	0.62 (0.53–0.71)

These results are robust to many changes in the dataset. For example, if the two combination arms of ONTARGET are omitted, the incoherence value decreases to 0.04721. In either scenario, the diuretic, beta-blocker, ACE-inhibitor, and ARB are significantly different than placebo in both network and Bayesian analyses. The rank ordering of drug classes for the association with new onset diabetes remains identical to that originally reported.

Keywords: New-onset diabetes mellitus; Thiazide-facilitated glucose intolerance; Network meta-analysis

PO-166

EFFICACY AND SAFETY OF COMBINATION DRI/CCB (± DIURETIC) IN US MINORITY PATIENTS WITH STAGE 2 HYPERTENSION AND OBESITY

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Obesity is a frequent comorbidity of hypertension that contributes to an increased activation of the renin-angiotensin system (RAS). Aliskiren is a direct renin inhibitor that acts on the RAS. Previously, in an 8-week, randomized, double-blind, forced-titration study in 411 self-identified US minority patients with stage 2 hypertension, we reported significant blood pressure (BP) lowering with combination aliskiren/amlodipine (A/AML) and that the addition of hydrochlorothiazide (HCTZ) further improved efficacy. This analysis reports data in 249 (60.6%) obese patients (baseline body mass index [BMI] ≥30 kg/m^2, mean age 53.6 years). Following a 1–4 week washout, eligible patients were randomized to A/AML 150/5 mg or AML 5 mg for 1 week.

MSSBP and MSDBP results in obese and non-obese patients

Parameter	Obese (BMI ≥30 kg/m^2) A/AML/HCTZ (n = 122)	Obese (BMI ≥30 kg/m^2) A/AML (n = 127)	Non-obese (BMI <30 kg/m^2) A/AML/HCTZ (n = 78)	Non-obese (BMI <30 kg/m^2) A/AML (n = 82)
Baseline MSSBP, mmHg (mean±SE)	166.6 ± 0.7	167.0 ± 0.6	167.9 ± 0.8	168.0 ± 0.8
Change from baseline to week 8, mmHg (LSM±SE)	-35.4 ± 1.2*†	-29.4 ± 1.2*	-37.8 ± 1.8*‡	-29.5 ± 1.8*
Baseline MSDBP, mmHg (mean±SE)	95.6 ± 0.8	95.9 ± 0.7	94.6 ± 1.0	94.2 ± 0.9
Change from baseline to week 8, mmHg (LSM±SE)	-14.3 ± 0.7*§	-11.9 ± 0.7*	-16.0 ± 1.1*§	-12.0 ± 1.1*

LSM, least-square mean; MSDBP, mean sitting diastolic blood pressure. *$P < 0.0001$; vs baseline. †$P < 0.001$, ‡ $P < 0.01$, § $P < 0.05$; vs A/AML.

LSM, least-square mean; MSDBP, mean sitting diastolic blood pressure. *$P < 0.0001$; vs baseline. †$P < 0.001$, ‡ $P < 0.01$, § $P < 0.05$; vs A/AML.

HCTZ was added to A/AML (A/AML/HCTZ 150/5/12.5 mg) and A was added to AML (A/AML 150/5 mg) for 1 week; force-titrated to A/AML/HCTZ 300/5/25 mg or A/AML 300/5 mg for 2 weeks; and to A/AML/HCTZ 300/10/25 mg or A/AML 300/10 mg for 4 weeks. At baseline, mean sitting systolic BP (MSSBP) was 166.8 mmHg in obese patients. At week 8, in this subgroup, combination A/AML significantly reduced BP from baseline (Table). Addition of HCTZ provided further significant reductions in MSSBP compared with A/AML (-35.4 mmHg vs -29.4 mmHg; $P < 0.001$). The most common adverse events in obese patients were headache (13.1% triple therapy, 7.9% dual therapy), diarrhea (1.6%, 4.7%), and dizziness (3.3%, 3.1%). In conclusion, combination A/AML therapy is effective in lowering BP in US minority patients with stage 2 hypertension and obesity; addition of HCTZ significantly improves efficacy.

Keywords: Hypertension; Aliskiren; Amlodipine; Hydrochlorothiazide

PO-167

EFFICACY OF COMBINATION ALISKIREN/AMLODIPINE (A/AML) WITH AND WITHOUT DIURETIC ON AMBULATORY BLOOD PRESSURE (ABP) IN MINORITIES WITH HYPERTENSION

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ABP is a better predictor of cardiovascular events than clinic BP. Previously, in an 8-week, randomized, double-blind, forced-titration study in 411 self-identified US minorities with stage 2 hypertension, we reported significant clinic BP-lowering with combination A/AML and that the addition of hydrochlorothiazide (HCTZ) further improved efficacy. Here we present results in the subset of 226 (55.0%) patients who underwent ABP monitoring. After a 1–4 week washout, eligible patients were randomized to A/AML 150/5 mg or AML 5 mg for 1 week. HCTZ was added to A/AML (A/AML/HCTZ 150/5/12.5 mg) and A was added to AML (A/AML 150/5 mg) for 1 week; force-titrated to A/AML/HCTZ 300/5/25 mg or A/AML 300/5 mg for 2 weeks; and to A/AML/HCTZ 300/10/25 mg or A/AML 300/10 mg for 4 weeks. At baseline, mean ambulatory systolic BP (SBP) was 148.8 mmHg. As observed for clinic BP, at week 8, combination A/AML significantly reduced 24-h ABP from baseline (Table). Addition of HCTZ provided further reductions, although not significant vs A/AML. Similar findings were observed for daytime SBP (-24.1 mmHg A/AML/HCTZ vs -20.8 mmHg A/AML) and last 6-h ambulatory SBP (-24.1 mmHg vs -20.8 mmHg) (both $P < 0.05$). Both treatments reduced systolic load (% ambulatory SBP readings >130 mmHg) from baseline ($P < 0.0001$); however, significantly greater reductions were observed with triple therapy vs dual therapy (-46.5% vs -39.2%; $P = 0.047$). As with clinic BP, combination A/AML effectively lowers 24-h ABP and systolic load in US minorities with stage 2 hypertension; addition of HCTZ improves efficacy.

Keywords: Hypertension; Aliskiren; Amlodipine; Hydrochlorothiazide

PO-168

ROLE OF PLASMA RENIN ACTIVITY ON BP RESPONSE TO ALISKIREN-BASED THERAPY IN STAGE 2 HYPERTENSIVE AFRICAN AMERICANS

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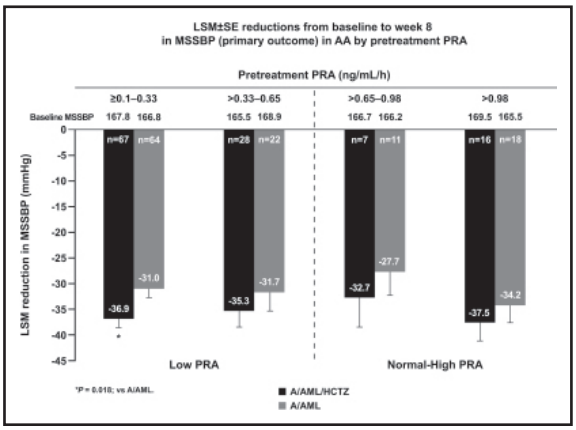
Low plasma renin activity (PRA) is common in hypertensive African Americans (AA), and drugs blocking the renin-angiotensin system (RAS) may be less effective in low-renin hypertension. (Ferdinand & Ferdinand 2008) Previous findings indicate that the blood pressure (BP) responses to treatment with aliskiren (A) in combination with a diuretic (hydrochlorothiazide [HCTZ]) or calcium channel blocker (amlodipine [AML]) are not predicted by pretreatment PRA.(Ferdinand et al 2010) In this 8-week, randomized, double-blind, forced-titration study, we evaluated the influence of pretreatment PRA on the clinic BP-lowering efficacy of dual (A/AML) and triple (A/AML/HCTZ) combination therapy in 256 AA (mean age 53.7 years) who were a subset of a study of 411 self-identified US minority patients with stage 2 hypertension. Following a 1–4 week washout, eligible patients were randomized to A/AML 150/5 mg or AML 5 mg for 1 week. HCTZ was added to A/AML (A/AML/HCTZ 150/5/12.5 mg) and A was added to AML (A/AML 150/5 mg) for 1 week; force-titrated to A/AML/HCTZ 300/5/25 mg or A/AML 300/5 mg for 2 weeks; and to A/AML/HCTZ 300/10/25 mg or A/AML 300/10 mg for 4 weeks. Among AA with available data, pretreatment PRA was ≤0.65 ng/mL/h for 181 (77.7%) patients and >0.65 ng/mL/h for 52 (22.3%) patients; mean sitting systolic BP (MSSBP) was 167.2 mmHg. At week 8, across pretreatment PRA levels, least-square mean (LSM) reductions from baseline in MSSBP ranged from -27.7 to -34.2 mmHg with A/AML and from -32.7 to -37.5 mmHg with A/AML/HCTZ (Figure). In conclusion,

24 h ABP and Clinic BP Results in ABP Subgroup

	24-h ABP		Clinic BP	
Parameter	A/AML/HCTZ (n = 112)	A/AML (n = 114)	A/AML/HCTZ (n = 113)	A/AML (n = 115)
Baseline SBP/DBP, mmHg (mean±SE)	148.3 ± 1.2/86.7 ± 1.0	149.3 ± 1.3/87.7 ± 1.0	167.8 ± 0.8/94.7 ± 0.8	167.7 ± 0.7/94.6 ± 0.8
Change from baseline to week 8, mmHg (LSM±SE)				
SBP/DBP	-23.4 ± 1.0*/-13.0 ± 0.7*	-20.5 ± 1.0*/-12.2 ± 0.7*	-36.0 ± 1.4*†/-14.9 ± 0.8*‡	-30.7 ± 1.3*/-12.3 ± 0.8*
Daytime SBP/DBP	-24.1 ± 1.1*‡/-13.7 ± 0.7*	-20.8 ± 1.1*/-12.3 ± 0.7*		
Nighttime SBP/DBP	-21.7 ± 1.1*/-11.6 ± 0.7*	-20.0 ± 1.1*/-11.8 ± 0.7*		
Last 6-h (18–24 hour) SBP/DBP	-24.1 ± 1.1*‡/-13.5 ± 0.8*	-20.8 ± 1.1*/-12.4 ± 0.8*		

LSM, least-square mean. *$P < 0.0001$; vs baseline. †$P < 0.01$, ‡$P < 0.05$; vs A/AML.

consistent with previous findings, our results show that most AA have low PRA. Aliskiren-based dual and triple therapies provide effective BP lowering in AA that is not influenced by pretreatment PRA.[figure1]



Keywords: Hypertension; Aliskiren; Amlodipine; Hydrochlorothiazide

PO-169

EFFICACY AND SAFETY OF COMBINATION DRI/CCB (±DIURETIC) THERAPY IN AFRICAN AMERICANS WITH STAGE 2 HYPERTENSION

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The updated International Society on Hypertension in Blacks (ISHIB) guidelines recommend the use of renin-angiotensin system (RAS) inhibitors in combination with calcium channel blockers or thiazide diuretics in African Americans (AA) when blood pressure (BP) is >15/10 mmHg above target. Triple therapy with these drug classes is a recommended next step. Previously, in an 8-week, randomized, double-blind, forced-titration study in 411 self-identified US minority patients with stage 2 hypertension, we reported significant BP lowering with combination aliskiren/amlodipine (A/AML) and that the addition of hydrochlorothiazide (HCTZ) further improved efficacy. In this post-hoc analysis, we report the efficacy and safety in 256 (62.3%) AA (mean age 53.7 years, mean body mass index 32.6 kg/m^2). Following a 1–4 week washout, eligible patients were randomized to A/AML 150/5 mg or AML 5 mg for 1 week. HCTZ was added to A/AML (A/AML/HCTZ 150/5/12.5 mg) and A was added to AML (A/AML 150/5 mg) for 1 week; force-titrated to A/AML/HCTZ 300/5/25 mg or A/AML 300/5 mg for 2 weeks; and to A/AML/HCTZ 300/10/25 mg or A/AML 300/10 mg for 4 weeks. At baseline, mean sitting systolic BP (MSSBP) was 167.2 mmHg. At week 8, combination A/AML significantly reduced BP from baseline (Table). Addition of HCTZ provided further significant reductions in MSSBP compared with A/AML (-36.6 mmHg vs -29.8 mmHg; $P < 0.001$). The most common adverse events were headache (11.9% triple therapy, 11.5% dual therapy) and diarrhea (2.4%, 4.6%). In conclusion, combination A/AML therapy is effective in lowering BP in AA with stage 2 hypertension; addition of HCTZ significantly improves efficacy.

MSSBP and MSDBP Results in AA

Parameter	A/AML/HCTZ (n = 126)	A/AML (n = 130)
Baseline MSSBP, mmHg (mean±SE)	167.3 ± 0.6	167.2 ± 0.6
Change from baseline to week 8, mmHg (LSM±SE)	-36.6 ± 1.3*†	-29.8 ± 1.3*
Baseline MSDBP, mmHg (mean±SE)	97.0 ± 0.8	97.1 ± 0.7
Change from baseline to week 8, mmHg (LSM±SE)	-15.6 ± 0.8*‡	-12.4 ± 0.8*

LSM, least-square mean; MSDBP, mean sitting diastolic blood pressure; SE, standard error. *$P < 0.0001$; vs baseline. †$P < 0.001$, ‡$P < 0.01$; vs A/AML.

Keywords: Hypertension; Aliskiren; Amlodipine; Hydrochlorothiazide

PO-170

COMBINATION ALISKIREN/AMLODIPINE (A/AML) WITH AND WITHOUT DIURETIC IN MINORITIES WITH HYPERTENSION AND METABOLIC SYNDROME (METS) OR DIABETES

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Hypertension frequently coexists with MetS and diabetes. Combination therapy with a renin-angiotensin system inhibitor along with a calcium channel blocker and/or diuretic has proven useful for management of these high-risk populations. Previously, in an 8-week, randomized, double-blind, forced-titration study in 411 self-identified US minority patients with stage 2 hypertension, we reported significant BP lowering with combination A/AML that was further improved by the addition of HCTZ. This analysis reports data in 284 (69.1%) MetS patients (mean age 55.0 years) and 118 (28.7%) diabetics (mean age 57.4 years). After a 1–4 week washout, eligible patients were randomized to A/AML 150/5 mg or AML 5 mg for 1 week. HCTZ was added to A/AML (A/AML/HCTZ 150/5/12.5 mg) and A was added to AML (A/AML 150/5 mg) for 1 week; force-titrated to A/AML/HCTZ 300/5/25 mg or A/AML 300/5 mg for 2 weeks; and to A/AML/HCTZ 300/10/25 mg or A/AML 300/10 mg for 4 weeks. At baseline, MSSBP was 167.4 mmHg in MetS patients and 167.1 mmHg in diabetics. At week 8, in MetS patients, combination A/AML significantly reduced BP from baseline (Table). Addition of HCTZ provided further significant reductions in MSSBP compared with A/AML (-35.2 mmHg vs -28.0 mmHg; $P < 0.0001$). Similar results were noted in diabetics. The most common adverse event in both subgroups was headache (MetS: 11.9% A/AML/HCTZ, 7.4% A/AML; diabetic: 11.1%, 9.1%). In conclusion, combination A/AML therapy is effective in lowering BP in US minority patients with stage 2 hypertension and MetS or diabetes; addition of HCTZ significantly improves efficacy.

Keywords: Hypertension; Aliskiren; Amlodipine; Hydrochlorothiazide

MSSBP and MSDBP Results in MetS and Diabetic Patients				
	MetS		Diabetic	
Parameter	A/AML/HCTZ (n = 135)	A/AML (n = 149)	A/AML/HCTZ (n = 63)	A/AML (n = 55)
Baseline MSSBP, mmHg (mean±SE)	167.1 ± 0.6	167.8 ± 0.6	166.7 ± 1.0	167.6 ± 1.0
Change from baseline to week 8, mmHg (LSM±SE)	-35.2 ± 1.3*†	-28.0 ± 1.2*	-35.5 ± 1.7*‡	-28.2 ± 1.8*
Baseline MSDBP, mmHg (mean±SE)	95.0 ± 0.8	95.3 ± 0.7	92.0 ± 1.2	93.3 ± 1.2
Change from baseline to week 8, mmHg (LSM±SE)	-14.9 ± 0.8*‡	-11.8 ± 0.7*	-14.2 ± 1.1*	-11.8 ± 1.1*
BP <140/90 mmHg at week 8, %	69.6‡	50.7	75.4§	55.8
LSM, least-square mean; MSDBP, mean sitting diastolic blood pressure. *$P < 0.0001$; vs baseline. †$P < 0.0001$, ‡$P < 0.01$, §$P < 0.05$; vs A/AML.				

LSM, least-square mean; MSDBP, mean sitting diastolic blood pressure. *$P < 0.0001$; vs baseline. †$P < 0.0001$, ‡$P < 0.01$, §$P < 0.05$; vs A/AML.

PO-171

EFFICACY AND SAFETY OF OLMESARTAN MEDOXOMIL VS LOSARTAN POTASSIUM IN SUBJECTS WITH STAGE 1 OR 2 HYPERTENSION

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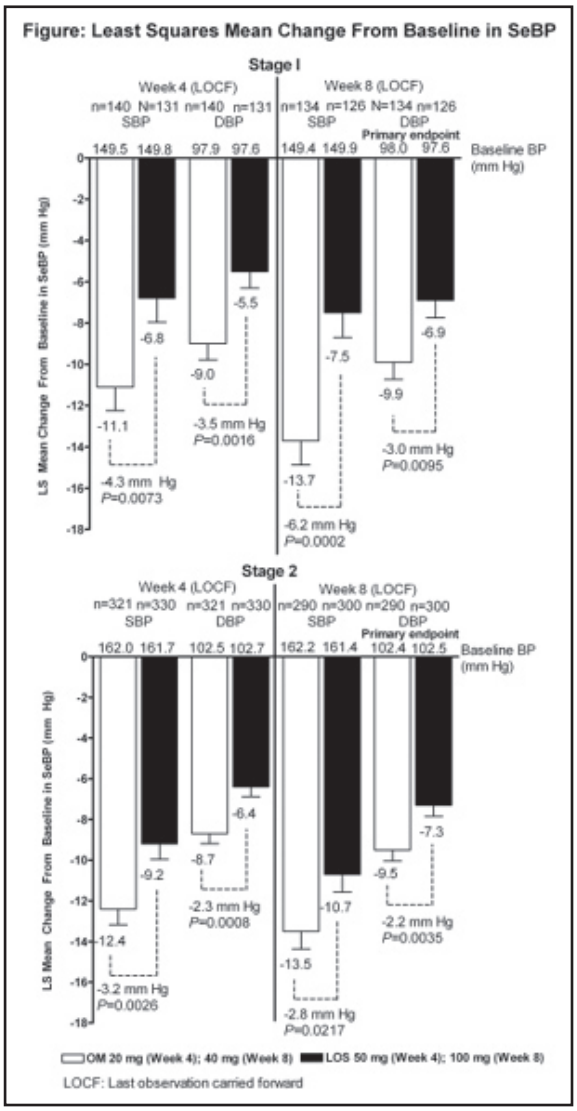
An exploratory subgroup analysis of a prospective, randomized, double-blind, forced-titration study of olmesartan medoxomil (OM) vs losartan potassium (LOS) in subjects (sbjs) with stage 1 or 2 hypertension (HTN) is reported. Study included 3–4 week (wk) placebo run-in and 8-wk active treatment (OM: Weeks 1–4 OM 20 mg, Weeks 5–8 OM 40 mg; Placebo + OM: Weeks 1–2 Placebo, Weeks 3–4 OM 20 mg, Weeks 5–8 OM 40 mg; LOS: Weeks 1–4 LOS 50 mg, Weeks 5–8 LOS 100 mg). Analyses focused on comparison of OM and Placebo + OM combined vs LOS. Efficacy endpoints were mean change from baseline in seated (Se) DBP at Wk 8 (primary), SeSBP at Wk 8, SeSBP and SeDBP at Wk 4 (secondary) and BP target achievement (tertiary). Randomized population comprised 941 sbjs with mean±SD age of 51.9 ± 9.7 years; 54.5% were male, 29.4% had stage 1 HTN and 70.6% had stage 2 HTN. For stage 1 sbjs baseline SeBPs (±SD) were 149.5 ± 6.7/97.9 ± 1.3 mmHg (OM) and 149.7 ± 7.1/97.6 ± 1.3 mmHg (LOS) and for stage 2 sbjs 162.0 ± 9.4/102.5 ± 4.0 mmHg (OM) and 161.8 ± 9.3/102.7 ± 4.0 mmHg (LOS). OM therapy lowered SeBP significantly more than LOS (Figure) and resulted in more sbjs with stage 1 or 2 HTN achieving target BP (Table).[figure1]

OM and LOS were well-tolerated. In the OM arm treatment-emergent adverse events (TEAE) occurred in 46/141 (32.6%) of stage 1 sbjs and in 99/324 (30.6%) of stage 2 sbjs compared with 43/134 (32.1%) of stage 1 sbjs and in 105/335 (31.3%) of stage 2 sbjs in the LOS arm. In the OM arm drug-related TEAEs occurred in 8 (5.7%) and 23 (7.1%) of stage 1 and 2 sbjs, respectively compared with 6 (4.5%) and 20 (6.0%) in the LOS arm.



Target Achievement <140/90 mmHg (%)						
	Week 4 LOCF		Week 8 LOCF		Overall	
Target	OM	LOS	OM	LOS	OM	LOS
Stage 1	43.6[a]	22.9	48.5[b]	29.4	63.6[b]	47.3
Stage 2	19.0[b]	10.9	23.8[b]	15.3	36.1[b]	25.2
[a]$P < 0.001$, [b]$P < 0.01$ vs LOS						

Keywords: Stage 1 and 2; Olmesartan medoxomil; Losartan; BP control

PO-172

DECREASING SLEEP-TIME BLOOD PRESSURE DETERMINED BY AMBULATORY MONITORING REDUCES CARDIOVASCULAR RISK IN RESISTANT HYPERTENSION

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Independent prospective studies have found that the sleep-time blood pressure (BP) mean is a better predictor of cardiovascular (CVD) risk than the awake or 24h BP means. A limitation of all

previous studies is their reliance on a single baseline ambulatory BP (ABPM) profile from each participant, without accounting for possible changes in the BP pattern or level during the years of follow-up. Thus, the potential reduction in CVD risk associated with specifically reducing asleep BP is yet to be documented. The MAPEC study was designed to test the hypothesis that bedtime chronotherapy with ≥1 hypertension medications exerts better BP control and CVD risk reduction than conventional therapy, i.e., all medications ingested in the morning. A total of 776 subjects with resistant hypertension, 387 men/389 women, 61.6 ± 11.2 yrs of age, were randomized to ingest all their hypertension medications upon awakening or ≥1 of them at bedtime. BP was measured by ABPM for 48h at baseline and again annually and more frequently (quarterly) if treatment adjustment was required. The median follow-up was 5.4 yrs (range 0.5 to 8.5 yrs). Subjects randomized to ingest ≥1 medications at bedtime experienced significantly better BP control during sleep as expressed by the enhanced reduction of the asleep BP mean and increased sleep-time relative BP decline towards a more dipping BP pattern. The decrease in sleep-time BP mean during follow-up was significantly associated with event-free survival (relative risk for each 5 mmHg decrease in sleep-time mean 0.89 [0.84–0.94]; $P < 0.001$). Moreover, the decrease in mean asleep BP during follow-up was the only parameter significantly associated with survival when other ABPM characteristics (including daytime BP mean, morning surge, or standard deviation) were simultaneously included in the Cox regression models. In resistant hypertension, the progressive reduction in the asleep BP mean from baseline was the most significant predictor of survival. Treatment at bedtime is the most cost-effective and simplest strategy of successfully achieving the therapeutic goals of adequate asleep BP reduction and preserving or re-establishing the normal 24h BP dipping pattern.

Keywords: Chronotherapy; Resistant hypertension; Cardiovascular risk; Sleep-time blood pressure

PO-173

INFLUENCE OF CIRCADIAN TIME OF BLOOD PRESSURE-LOWERING TREATMENT ON CARDIOVASCULAR RISK IN RESISTANT HYPERTENSION

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In resistant hypertension, ingesting one blood pressure (BP)-lowering medication at bedtime, as compared to treatment with all medications upon awakening, has been shown to be associated with a 40% increased BP control, a significant reduction of sleep-time BP, and the corresponding remodeling of the BP pattern towards a more dipping profile. However, the potential differential reduction of cardiovascular (CVD) risk by a bedtime vs upon-awakening treatment schedule in resistant hypertension has never been evaluated prospectively. The MAPEC study was specifically designed to test the hypothesis that bedtime chronotherapy with ≥1 hypertension medications exerts better BP control and CVD risk reduction than conventional therapy, i.e., all medications ingested in the morning. A total of 776 subjects with resistant hypertension, 387 men/389 women, 61.6 ± 11.2 yrs, were randomized to ingest all their hypertension medications upon awakening or ≥1 of them at bedtime. At baseline, BP was measured by ambulatory monitoring for 48h. Physical activity was simultaneously monitored every min by wrist actigraphy. Identical assessment was scheduled annually and more frequently (quarterly) if treatment adjustment was required. The Cox proportional-hazard model was used to estimate relative risk of CVD events. The median time of follow-up was 5.4 yrs (range 0.5 to 8.5 yrs). The Kaplan-Meier survival curves indicate a highly significant difference between timed-treatment groups in event-free survival (log-rank 29.2, $P < 0.001$). Subjects ingesting ≥1 BP-lowering medications at bedtime evidenced a significantly lower relative risk of total events than subjects ingesting all of their medications upon awakening (relative risk 0.38; 95% confidence interval [0.27–0.55]; $P < 0.001$). Particularly relevant is the difference between the two treatment-time groups in the adjusted relative risk of major CVD events, i.e., CVD deaths, myocardial infarction, ischemic stroke, and hemorrhagic stroke (0.35 [0.18–0.68]; $P = 0.002$). In resistant hypertension, pharmacological therapy should take into account when to treat with respect to the rest-activity cycle of each individual subject. Bedtime chronotherapy with ≥1 BP-lowering medications, compared to conventional upon-waking treatment with all medications, more effectively improved BP control and significantly reduced CVD morbidity and mortality.

Keywords: Chronotherapy; Resistant hypertension; Cardiovascular risk

PO-174

ADMINISTRATION-TIME DIFFERENTIAL BENEFIT ON CARDIOVASCULAR RISK REDUCTION OF THE VARIOUS CLASSES OF HYPERTENSION MEDICATIONS

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Clinical studies have documented morning-evening, administration-time differences of several classes of hypertension medications in blood pressure (BP)-lowering efficacy, duration of action, safety profile, and/or effects on the circadian BP pattern. The MAPEC study has also documented that bedtime chronotherapy with ≥1 BP-lowering medications, compared to conventional upon-waking treatment with all medications, more effectively improved BP control, better decreased the prevalence of non-dipping, and, most importantly, significantly reduced cardiovascular (CVD) morbidity and mortality. We further evaluated a potential administration-time differential benefit on CVD risk reduction of the various classes of medications prescribed in the MAPEC prospective trial. A total of 2156 hypertensive subjects, 1044 men/1112 women, 55.6 ± 13.6 yrs of age, were randomized to ingest all their hypertension medications upon awakening or ≥1 of them at bedtime. This randomization was done separately for each allowed individual hypertension medication. BP was measured for 48h at baseline and again annually or more frequently (quarterly) if treatment adjustment was required. The median follow-up was 5.6 yrs (range 0.5 to 8.6 yrs). Subjects treated at bedtime evidenced a significantly lower relative CVD risk (adjusted by sex, age and diabetes) than subjects treated upon awakening, independently of the class of medication. Greater benefits were observed for bedtime compared to awakening treatment with ARB (relative risk 0.29 [0.17–0.51]; $P < 0.001$) and CCB (0.46 [0.31–0.69]; $P < 0.001$). For subjects treated upon awakening, CVD risk was similar for the various classes of medications. For treatment at bedtime, however, ARBs were significantly superior in terms of CVD risk reduction as compared to all other classes (CVD risk relative to ARB of 2.64 for ACEI, 2.11 for CCB, 2.77 for alpha-blocker, 3.26 for beta-blocker, and 2.35 for diuretics; P always <0.017). Bedtime chronotherapy significantly reduces CVD risk compared to conventional morning dosing independently of the class of BP-lowering medication used for treatment. Results show no advantage of any particular class of

medication in terms of CVD morbidity and mortality when treatment is administered upon awakening. ARBs, however, are significantly superior to any other medications when treatment is administered at bedtime.

Keywords: Chronotherapy; Cardiovascular risk; Hypertension treatment

PO-175

INFLUENCE OF NUMBER OF HYPERTENSION MEDICATIONS AND CIRCADIAN TIME OF TREATMENT ON CARDIOVASCULAR MORBIDITY AND MORTALITY

Ramon C. Hermida, Diana E. Ayala, Artemio Mojon, Jose R. Fernandez. University of Vigo, Vigo, Spain.

In a number of observational studies (presumably on populations treated in the morning), subjects on antihypertensive medication were found to have worse prognosis that untreated hypertensives. The most likely explanations are unsuccessful blood pressure (BP) control and the fact that subjects with severe hypertension are more likely to receive more treatment than lower-risk hypertensives. We investigated the influence on cardiovascular (CVD) risk of the number of medications and time of treatment in the MAPEC study, specifically designed to test if bedtime chronotherapy with $\geq$1 hypertension medications exerts better BP control and CVD risk reduction than conventional therapy, i.e., all medications ingested in the morning. A total of 2156 hypertensive subjects, 1044 men/1112 women, 55.6 $\pm$ 13.6 yrs of age, were randomized to ingest all their hypertension medications upon awakening or $\geq$1 of them at bedtime. BP was measured for 48h at baseline and again annually or more frequently (quarterly) if treatment adjustment was required. CVD risk according to number of medications used at the final evaluation was calculated by comparison with 734 normotensive subjects who were identically followed and remained untreated. The median follow-up was 5.6 yrs (range 0.5 to 8.6 yrs). In hypertensive subjects treated with all medications upon awakening, CVD risk was progressively higher with incremental number of agents used for treatment (1.75, 2.26, 3.02, and 4.18 in patients treated with 1, 2, 3 or $\geq$4 medications, respectively; $P < 0.001$ compared to normotensive subjects). CVD risk was markedly lower in subjects treated with $\geq$1 medications at bedtime (0.35, 1.45, 0.94, and 2.28 with 1, 2, 3 or $\geq$4 total ingested medications). CVD risk was even lower, and always statistically comparable to that of normotension, when subjects were treated with al medications at bedtime (0.35, 0.39, 0.87, and 0.79 with 1, 2, 3 or $\geq$4 medications). Pharmacological therapy of hypertension should take into account when to treat with respect to the rest-activity cycle of each individual subject. Bedtime chronotherapy has been shown to more effectively control asleep BP and thus significantly reduce CVD risk. These novel results challenge the common believe of a residual CVD risk among hypertensive subjects that cannot be properly reduced by pharmacotherapy with available hypertension medications.

Keywords: Chronotherapy; Cardiovascular risk

PO-176

DOPPLER MEASUREMENT OF ANKLE BRACHIAL INDEX IS STILL THE STANDARD IN SCREENING OF PERIPHERAL ARTERIAL DISEASE?

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Ankle-brachial index (ABI) is a noninvasive screening test for peripheral arterial disease (PAD). The golden standard for measurement of ABI is a hand-held Doppler stethoscope for auscultation of both dorsal pedal (ADP) and posterior tibial artery (ATP) pulses.

The aim of this study was to find an easy method for the measurement of ABI by comparing the oscillometric device aimed for BP measurement (Omron M3 Intellisense, HEM-7051-E, Kyoto, Japan) (OscM) to the Doppler stethoscope (Model 841-A, Parks Medical Electronics Inc, USA) (DopM).

One hundred diabetic patients (aged 18–81 years, mean GHbA1c 7.8 (1.5) %) were enrolled in the study. A single observer (LR) measured the ABI using both methods.

Mean ABI in the right side was 1.10 (0.17) and 1.13 (0.20) in the left side with DopM and correspondingly 1.13 (0.15) and 1.13 (0.12) with the OscM (p=ns). ABI was abnormal (either <0.9 or >1.3) in 24 patients with the DopM and in 20 patients with the OscM. Compared to Doppler method, OscM found 8 false positive and 12 true positive. ABI was normal in 175 ankles with the OscM, 21 of them were false negative (17 patients). The positive predictive value of OscM was 64% and the negative predictive value 88%, DopM as a golden standard. The sensitivity and specificity of the OscM were 43% and 94%. Palpating the pulses and testing for limited joint mobility (LJM) of the hand gives 20 true positive and 23 false positive, 53 true negative and 4 false negative which gives testing both the pulses and LJM a positive predictive value 46.5%, a negative predictive value 93.0% and a sensitivity 83.3% and specificity 69.7%.

The OscM in measuring the ankle pressure was not sensitive enough for screening PAD in diabetic patients. It would have missed half of the patients with an abnormal ABI. Therefore we cannot recommend using the Omron M3 blood pressure device in measuring the ankle pressure as a PAD screening method in diabetic patients. In our study palpating the ADP pulses and testing for LJM was a better method for screening PAD than the OscM. Thus DopM stays still the standard method for screening PAD in diabetic patients if it is available.

Keywords: Peripheral arterial disease; Measurement; Doppler; Oscillometric

PO-177

COMPARATIVE EFFECTS OF CARVEDILOL AND VALSARTAN ON CARDIAC WORKLOAD

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Background: Guidelines recommend the use of beta-blockers and ACE inhibitors in ischemic heart disease. We investigated whether sustained-release carvedilol (C) was superior to valsartan (V) in reducing cardiac workload when added to background ACE inhibitor therapy for essential hypertension.

Methods: After a 3-week baseline of lisinopril 40 mg/day, subjects were randomized to receive two 4-week forced-titration, single-blinded periods of C (20 to 40 mg/day) or V (160 to 320 mg/day) in a randomized crossover design. At the end of the baseline and experimental periods, subjects had: (1) arterial tonometry (Sphygmocor) to determine cardiac time-tension index (CTTI, an index of cardiac load) at rest and after supine bicycle exercise, and (2) ambulatory BP monitoring (ABPM) to determine 24-hour "double product" (mean systolic BP x mean HR).

Results: 30 subjects completed the study. Primary results [mean(SD)] are shown in Table I. CTTI correlated well with SBP*HR (r = 0.92, $P < 0.000$).

	Rest			Bicycle (60 watts)			24-hr ABPM		
	CTTI	HR	SBP	CTTI	HR	SBP	SBP*HR	HR	SBP
b	2684(453)	72(13)	150(18)	3800(836)	113(23)	168(27)	11127(2900)	79(15)	141(14)
V	2500(561)	75(17)	143(24)	3597(984)	113(24)	163(33)	10295(2900)†	78(14)	132(19)
C	2447(547)††	68(14)**††	147(26)	3612(967)	116(36)	161(33)	9870(2192)††	73(14)*††	135(19)

Conclusion: Compared to V, C reduced HR at rest and over 24 hours. C was not superior to V in lowering any of the indexes of cardiac work (CTTI at rest and after exercise or SBP*HR over 24 hours) but C did demonstrate a small effect on resting CTTI when compared to baseline.

Keywords: Carvedilol; Valsartan; Hemodynamics

PO-178

OLMESARTAN + CCB VS OLMESARTAN + DIURETIC AS COMBINATION THERAPY FOR ELDERLY HYPERTENSIVE PATIENTS

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The blood pressure goals set for the treatment of hypertensive patients have been lowered in recent guidelines. To reduce blood pressure levels sufficiently, combination therapies are often needed, but there is little evidence about which combination should be chosen. This study was carried out to compare the effects of combination therapies with the ARB olmesartan plus a dihydropyridine CCB or thiazide diuretic in elderly patients with hypertension. We recruited patients aged 65 to 85 years with essential hypertension with blood pressure levels of 140/90 mmHg or higher for those on anti-hypertensive medication, or 160/100 mmHg or higher not on medication. Patients were eligible if they had any of impaired glucose tolerance, diabetes, dyslipidemia, proteinuria, left ventricular hypertrophy, ischemic heart disease, or stroke, while those with a serum creatinine level of 2.0 mg/dl or higher were excluded from the study. Sixty-five patients were randomly assigned to either group treated with olmesartan plus a CCB or a diuretic, and 58 completed the treatment for 6 months. Systolic and diastolic blood pressure (SBP and DBP) were reduced during the treatment period in both groups, while the reductions in SBP at 1 and 6 months were significantly ($P < 0.05$) greater in the CCB combination group than in the diuretic group (-29 vs -18 mmHg at 1 month; -32 vs -23 mmHg at 6 months). Despite the greater reduction in SBP in the CCB group, the serum creatinine level and estimated glomerular filtration rate (eGFR) remained unchanged, while in the diuretic group creatinine was elevated (+0.06 mg/dl, $P < 0.05$) and eGFR was reduced (-4.5 ml/min/1.73 m^2, $P < 0.05$). In addition, high density lipoprotein cholesterol levels were reduced in the diuretic group (-5.0 mg/dl, $P < 0.01$). Plasma renin activities increased and aldosterone concentrations decreased in both groups ($P < 0.05$), but no differences were noted between the two groups. Plasma brain natriuretic peptide levels remained unchanged in either group. These results suggest that olmesartan plus a CCB is a preferable combination therapy in comparison with olmesartan plus a thiazide diuretic for elderly patients with hypertension.

Keywords: Angiotensin receptor blocker; Calcium channel blocker; Diuretic; Combination therapy

PO-179

EFFICACY AND SAFETY OF OLMESARTAN MEDOXOMIL VS LOSARTAN POTASSIUM IN ANTIHYPERTENSIVE NAÏVE/NON-NAÏVE SUBJECTS

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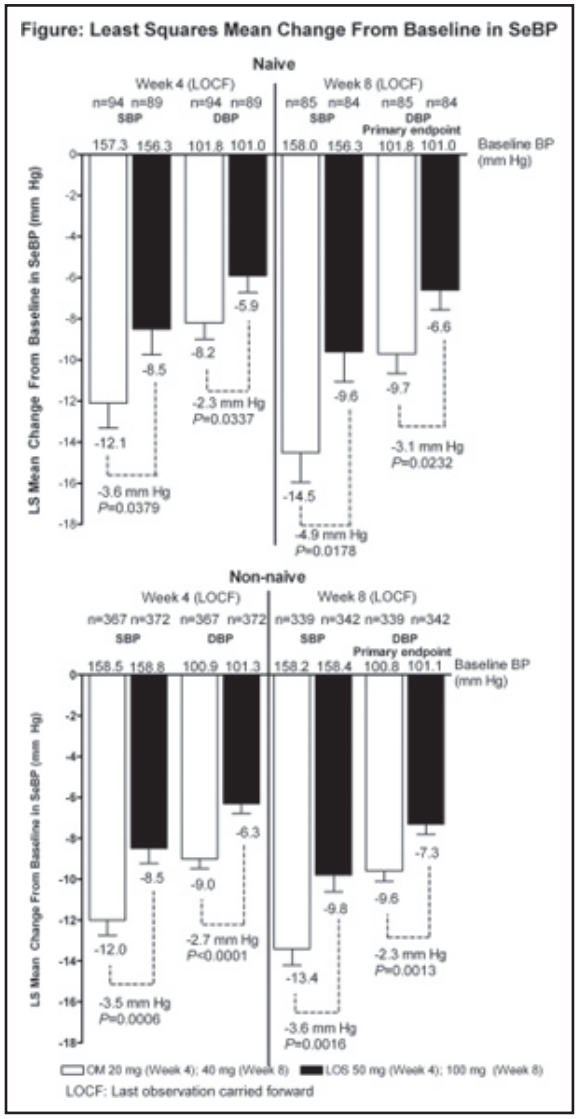
An exploratory subgroup analysis of a prospective, randomized, double-blind, forced-titration study of olmesartan medoxomil (OM) vs losartan potassium (LOS) in subjects (sbjs) with hypertension (HTN) not previously (naïve) or previously (non-naïve)



treated with antihypertensive medication is reported. Study included 3–4 week (wk) placebo run-in and 8-week active treatment (OM: Weeks 1–4 OM 20 mg, Weeks 5–8 OM 40 mg; Placebo + OM: Weeks 1–2 Placebo, Weeks 3–4 OM 20 mg, Weeks 5–8 OM 40 mg; LOS: Weeks 1–4 LOS 50 mg, Weeks 5–8 LOS 100 mg). Analyses focused on comparison of OM and Placebo + OM combined vs LOS. Efficacy endpoints were mean change from baseline in seated (Se) DBP at Week 8 (primary), SeSBP at Week 8, SeSBP and SeDBP at Week 4 (secondary) and BP target achievement (tertiary). Randomized population comprised 941 sbjs with mean ± sd age of 51.9 ± 9.7 years; 54.5% were male, 20.1% were naïve to antihypertensive medication. For naïve sbjs baseline SeBPs (±SD) were 157.4 ± 10.9/101.8 ± 4.3 mmHg (OM) and 156.3 ± 10.8/101.1 ± 3.9 mmHg (LOS) and for non-naïve sbjs 158.4 ± 10.2/100.9 ± 4.0 mmHg (OM) and 158.8 ± 10.1/101.3 ± 4.2 mmHg (LOS). OM therapy lowered SeBP significantly more than LOS (Figure) and resulted in more sbjs achieving target BP irrespective of whether previously treated with antihypertensives (Table).[figure1]

OM and LOS were well-tolerated. In the OM arm treatment-emergent adverse events (TEAE) occurred in 29/95 (30.5%) of naïve sbjs and in 116/370 (31.4%) of non-naïve sbjs compared with 30/91 (33.0%) of naive sbjs and in 118/378 (31.2%) of non-naïve sbjs in the LOS arm. In the OM arm drug-related TEAEs occurred in 8 (8.4%) and 23 (6.2%) of naïve and non-naive 1 and 2 sbjs, respectively compared with 3 (3.3%) and 23 (6.1%) in the LOS arm.

Target Achievement <140/90 mm Hg(%)						
	Week 4 LOCF		Week 8 LOCF		Overall	
Target	OM	LOS	OM	LOS	OM	LOS
Naive	22.3[b]	9.0	34.1[c]	19.0	42.6[c]	27.0
Non-naive	27.5[a]	15.6	31.0[a]	19.6	45.0[a]	32.5

[a]$P<0.001$, [b]$P<0.01$, [c]$P<0.05$ vs LOS

Keywords: Treatment naive/non-naive; Olmesartan medoxomil; Losartan; BP control

PO-180

COMPUTER-MEDIATED SYSTEM, WHEELS-I, PROVIDES EVIDENCE OF FEASIBILITY FOR MOMENTARY ASSESSMENT OF DASH DIET ADHERENCE OVER 8 WEEKS

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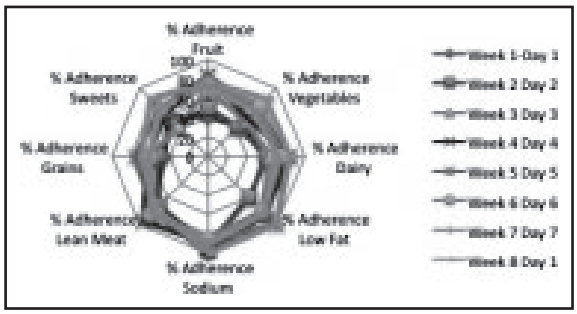
Background: The most modifiable lifestyle risk factor related to hypertension management is adherence to a heart health diet. DASH Diet is widely recommended as a healthy eating plan for hypertensive adults. Research is limited for reliable daily tracking of momentary dietary adherence measures that are useful for clinical practice to promote sustainable life long dietary behavior changes.

Objectives: We examined: 1. feasibility of DASH adherence scales involving daily momentary real time assessment, and 2. usefulness of radar plotting to represent variation of DASH adherence over time.

Methods: This is a sub-study of WHEELS-I, a clinical trial conducted with 70 women (74% African American, ages 35 to 76) seen at outpatient clinics and randomly assigned to experimental (CBI) or control groups (CG). The CBI group (n = 35) was exposed to email messages, 28 morning and 56 evening linked to web-based rapid response surveys. This study reports on the evening messages linked to DASH adherence survey assessing portion control recommendations for fruit, vegetables, low fat, low-fat dairy, limited sodium, lean meat, grains, and limited sweets; required 5 min to complete. The WHEELS-I computer interactive system was developed to link web-based random coded self appraisal survey data captured for statistical analyses.

Results: Delivery and tracking statistics revealed 2,924 messages were opened and 2,280 clicks to access web-based surveys over 8 weeks; an acceptable 78% intervention engagement profile. The average % DASH adherence for Weeks 1 and 8 displayed in the Radar Plot was 86.[figure1]The Radar Plot shows the dramatic improvement in % DASH adherence for fruit (42 to 77); vegetables (46 to 85); grains (46 to 69) and limited sweets (58 to 85).

Conclusions: This study showed a reliable technological approach for advancing systematic implementation of DASH in clinical practice; foundation is set for electronic medical record linkages and sharing Radar Plots with patients.



Keywords: DASH diet; Adherence; Momentary assessment; Radar plotting

PO-181

CARVEDILOL REDUCES AORTIC WAVE REFLECTION AND IMPROVES LEFT VENTRICULAR/VASCULAR COUPLING COMPARED TO ATENOLOL: THE CENTRAL STUDY

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Blood pressure (BP) characteristics, such as central aortic pressure and arterial stiffness, independently predict cardiovascular events and the effects of pharmacologically dissimilar β-blockers on these properties have not been fully elucidated.

Patients with essential hypertension and without significant concomitant cardiovascular disease were randomly assigned to controlled-release carvedilol, force-titrated to 80 mg (n = 22), or atenolol, force-titrated to 100 mg (n = 19); each was given once daily for four weeks. Radial artery applanation tonometry was used to derive central aortic BP and wave reflection properties from seated brachial BP attained conventionally using brachial sphygmomanometry.

Patients in both arms were similar except that mean height was 5.4 cm greater in carvedilol-treated patients vs atenolol-treated

patients (P = 0.04). At the end of week 4, atenolol and carvedilol reduced central and brachial systolic and diastolic BP to a similar extent. Pulse pressures followed the same trend. Central augmentation index (AIx) was increased in atenolol-treated patients but not carvedilol-treated patients (atenolol, 4.47% vs carvedilol, −0.68%; P = 0.04 for the comparison between changes). Mean augmented central aortic pressure increased slightly during atenolol treatment (+1.1 mmHg change from baseline), but decreased slightly during carvedilol treatment (-1.1 mmHg change from baseline), although the difference in these changes was not statistically significant (P = 0.23). Pulse pressure amplification ratio (PP amplification) was reduced more with atenolol at week four (atenolol, -10.7% vs carvedilol, -1.8%; P = 0.02).

Carvedilol and atenolol elicit similar reductions in central and brachial systolic and diastolic BP. However, carvedilol elicits a more favorable effect on several central hemodynamic characteristics, likely through its vasodilating properties on peripheral vascular beds. Carvedilol results in more favorable PP amplification and Aix by increasing arterial compliance and reducing the magnitude of wave reflection, respectively, compared to atenolol.

Keywords: Carvedilol; Atenolol; Essential hypertension; Central aortic blood pressure

PO-182

FIXED-DOSE COMBINATION OF AZILSARTAN MEDOXOMIL/CLD PROVIDES SUPERIOR BP REDUCTION TO MONOTHERAPIES IN STAGE 2 HTN

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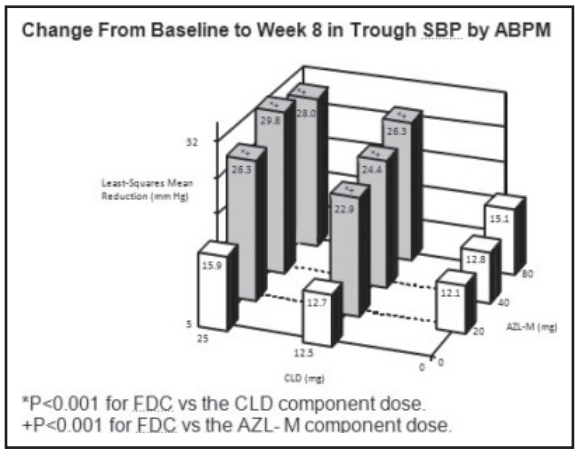
Background: We compared the efficacy and safety of various fixed-dose combinations (FDCs) of azilsartan medoxomil (AZL-M) and chlorthalidone (CLD) with individual monotherapies in patients with stage 2 hypertension.

Methods: In an 8-week, double-blind factorial study, 1714 subjects with clinic systolic BP (SBP) ≥160 and ≤190 mm Hg were randomized to AZL-M 0, 20, 40 or 80 mg and/or CLD 0, 12.5 or 25 mg, but with no double-placebo arm. The primary efficacy endpoint was change from baseline to week 8 for trough (hour 22–24) SBP by 24-hour ambulatory BP monitoring (ABPM). Trough seated clinic BP was also measured.

Results: Subjects' mean age was 57 years, 47% were men, 20% were black. Baseline trough BP was ≈165/95 mm Hg and ≈152/90 mm Hg by clinic and ABPM measurements, respectively. Each of the 6 AZL-M/CLD FDCs reduced trough SBP by ABPM more effectively than component monotherapy doses (P < 0.001) (Figure). Clinic BP reduction for AZL-M/CLD ranged from 33.8/14.4 to 40.1/18.5 mm Hg for the 20/12.5 to 80/25 mg doses, respectively. Discontinuation rates and elevations in serum creatinine occurred more commonly and in a dose-dependent manner with AZL-M/CLD. CLD-related hypokalemia was attenuated when combined with AZL-M as a FDC.

Conclusion: FDCs of AZL-M and CLD substantially reduced clinic and ambulatory SBP compared to the individual therapies in patients with stage 2 hypertension. Reversible creatinine elevations with AZL-M/CLD were related to the level of BP reduction in a small proportion of patients and were consistent with the extended diuretic effect of CLD and renin-angiotensin blockade due to AZL-M.[figure1]



Keywords: Hypertension; Azilsartan medoxomil; Chlorthalidone; Fixed-dose combination

PO-183

EFFICACY OF AN AMLODIPINE/OLMESARTAN MEDOXOMIL ALGORITHM IN PATIENTS UNCONTROLLED ON PRIOR ACE INHIBITOR MONOTHERAPY

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A prospective, open-label dose-titration study was conducted to assess the efficacy of an amlodipine/olmesartan medoxomil (AML/OM) treatment regimen in patients (pts) uncontrolled on monotherapy (SBP ≥140 mmHg [≥130 mmHg for pts with diabetes] and ≤180 mmHg and DBP ≤110 mmHg) Pts were switched without washout to AML/OM 5/20 mg and uptitrated every 4 weeks to AML/OM 5/40 mg, AML/OM 10/40 mg (to achieve seated (Se)BP <120/70 mmHg), AML/OM 10/40 + hydrochlorothiazide (HCTZ) 12.5 mg, and AML/OM 10/40 + HCTZ 25 mg (to achieve SeBP <125/75 mmHg). The primary endpoint was the percentage of pts achieving cumulative SeSBP goal <140 mmHg (<130 mmHg in diabetes) by Week 12. This is a prespecified subgroup analysis of pts on ACE inhibitor monotherapy. Of 999 patients, 289 pts were uncontrolled on prior ACE inhibitor monotherapy with a mean age (±SD) of 55.5 ± 12.0 years, baseline BP of 153.4 ± 9.5/91.5 ± 8.8 mmHg, and BMI of 30.9 ± 6.2 kg/m^2. The primary endpoint was achieved by 73.1% of pts in this subgroup. Other cumulative and noncumulative goals are showed in the Table.

Mean changes (±SE) from baseline in BP during the titration periods ranged from -15.1 ± 0.7/-8.2 ± 0.5 mmHg for AML/OM 5/20 mg to -24.1 ± 1.2/-13.3 ± 0.7 mmHg for AML/OM 10/40 + HCTZ 25 mg (all P < 0.0001 vs baseline). By week 20 a cumulative BP goal of <140/90 mmHg was achieved by 83.0% of pts. An ABPM study of a subset of patients demonstrated that BP reductions were maintained throughout the 24-hr dosing interval. Treatment emergent adverse events (TEAEs) occurred in 157/289 (54.3%) and drug-related (DR) TEAEs in 74/289 pts.

The majority of TEAEs were mild-to-moderate in severity. This well-tolerated treat-to-goal treatment algorithm allowed a large proportion of patients who previously were uncontrolled on ACE inhibitor monotherapy to safely achieve BP control by Week 12 and 20 on an amlodipine/olmesartan-based regimen.

Table

Goal Achievement:	Cumulative[a] Week 12 (%)	Noncumulative[b] Week 12 (LOCF) (%)
SeSBP (<140 mmHg; < 130 mmHg diabetes)	73.1[c]	61.1
SeBP (<140/90 mmHg; <130/80 mmHg diabetes)	69.3	57.6
Goal Achievement:	Cumulative Week 20 (%)	Noncumulative Week 12 (LOCF) (%)
SeBP (<140/90 mmHg; <130/80 mmHG diabetes)	83.0	72.1

[a]At any time point; [b]At visit; [c]Primary endpoint: LOCF: Last observation carried forward

Keywords: Olmesartan medoxomil; Amlodipine; BP control; Prior ACE inhibitor monotherapy

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PO-184

PILOT RANDOMIZED CONTROLLED TRIAL OF INTENSIVE BLOOD PRESSURE CONTROL IN HEMODIALYSIS DIALYSIS PATIENTS: THE BID TRIAL

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Studies in the general population have demonstrated the benefits of intensive control of hypertension. In contrast, hemodialysis (HD) patients who meet the National Kidney Foundation's guideline of a pre-dialysis blood pressure (BP) of < 140/90 mm Hg may have increased mortality vs patients with higher BP values. Moreover, there is large intra-individual variation in routine dialysis unit BP measurements (RDUBPM) leading some investigators to recommend that standardized dialysis unit (SDUBPM), home (HBPM) and ambulatory BP measurements (ABPM). BP measurements should guide antihypertensive therapy in HD patients. A randomized controlled trial comparing intensive vs standard hypertension control in HD patients is needed to assess the safety and efficacy of the KDOQI guideline. Given the complexity of conducting a full-scale trial we will conduct a pilot study entitled Blood Pressure in Dialysis (BID) Trial, co-sponsored by NIH and Dialysis Clinics Incorporated (DCI), a not-for profit provider.

The primary goal is to demonstrate feasibility and safety of conducting a full-scale trial in which participants would be treated to pre-dialysis standardized systolic BP of 110–140 (SBP) vs 155–165 mm Hg. Secondary goals include assessing the feasibility of collecting SDUBPM as well as HBPM and ABPM and comparing these to RDUBPM. BID will be the first randomized controlled trial in which antihypertensive therapy will be guided by SDUBPM.

Potential participants will undergo a baseline period with back-titration of antihypertensive agents to achieve a standardized SBP >155 mm Hg. Participants who meet eligibility criteria will be randomly assigned in a 1:1 allocation to the intensive or standard treatment arm. RDUBPM will be performed as standard of care. Weekly HBPM and quarterly ABPM will be performed. We will use a stepped care algorithm that consists of sodium and fluid restriction, reduction in dry weight and up-titration of antihypertensive agents. We will compare the changes in left ventricular mass, measured by cardiac MRI. The Cleveland Clinic Foundation and Brigham and Women's Hospital will serve as the Data Coordinating and Cardiac MRI Reading Centers, respectively.

Keywords: Blood pressure in hemodialysis patients; BP targets in hemodialysis patients; Hypertension in hemodialysis patients

Coronary Artery Disease

PO-185

BLOOD PRESSURE AND HEART RELATED QUALITY OF LIFE ONE YEAR POST MYOCARDIAL INFARCTION

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The purpose of the study was to assess the possible relationship of blood pressure (BP) and the health related quality of life (HRQoL) one year after acute myocardial infarction (AMI) as onset manifestation of coronary artery disease (CAD). The sample consisted of 112 AMI survivors who satisfied all inclusion

BP SUBGROUPS: HRQoL, BP AND OTHER PARAMETERS

PARAMETER	GROUP A (N:34)	B (N:49)	C (N:29)	*p* x
HRQoL				
15D	0.833	0.845	0.843	NS
MN *emotional*	5.49	5.53	5.67	NS
MN *physical*	5.28	5.48	5.52	NS
MN *social*	5.38	5.69	5.74	0.060
MN *global*	5.29	5.43	5.59	0.064
BLOOD PRESSURE				
SBP	109	126	143	<0.001
DBP	69	74	81	<0.001
PP	39	52	62	<0.001
MBP	89	100	112	<0.001
HEART RATE	68	69	65	NS
CRP	3.2	5.7	3.5	0.001
ESR	19	22	19	NS
proBNP	1551	1218	1125	0.022
EF	57	55	60	NS
AGE	66.4	64.9	60.8	0.062
GENDER				NS
MALE	26	36	23	
FEMALE	8	13	6	
AMI TYPE				NS
STEMI	16	21	11	
NSTEMI	18	28	18	
CAD RISK FACTORS				
HYPERTENSION	14	30	25	0.001
DYSLIPIDAEMIA	19	20	19	NS
DIABETES	10	10	7	NS
SMOKING	14	17	16	NS
FAMILY HISTORY	4	9	10	0.074
KILLIP CLASS				<0.001
I	13	18	21	
II	13	23	4	
III	8	6	0	
IV	0	2	4	
REVASCULARIZATION METHOD				0.024
NONE	4	10	0	
PCI	23	25	15	
CABG	7	14	14	

criteria and consented to participate in the research during the one year post-AMI follow up visit. HRQoL was measured with a generic and a disease specific instrument, the 15D and the MacNew HRQoL questionnaire in heart disease respectively. BP was measured according to international guidelines. Statistical analysis was conducted with SPSS with $P < 0.05$ as accepted level of significance. HRQoL scores did not show correlation with Systolic BP (SBP), Diastolic BP (DBP), Pulse Pressure (PP) and Mean BP (MBP). Patients with history of HTN (prior to AMI) reported poorer HRQoL with both instruments, yet not statistically significant (NSS). Surprisingly, when patients were classified into 3 groups according to SBP (A: SBP < 120, B: 120 ≤ SPB<140, and C: SBP≥140), group A reported lower HRQoL with both instruments and group C higher with MacNew, though NSS in all cases. Analysis between the three groups revealed statistical significant differences in prior history of HTN, in levels of CRP and proBNP, in Killip class, and in the type of revascularization. One possible explanation is that better control of HTN is achieved in more severe cases of CAD patients and therefore with lower level of HRQoL. Further analysis is needed to confirm the paradox that AMI survivors with high BP report higher HRQoL.

Keywords: Hypertension; Quality of life; Myocardial infarction

PO-186

FALSE-POSITIVE STRESS TESTING RESULTS IN HYPERTENSIVES WITH NO CORONARY ARTERY DISEASE

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Background: Hypertensives without significant angiographically defined coronary artery disease (CAD) have higher than expected false positive rates by non-invasive stress testing. The influence of baseline test findings were investigated as the possible resources of this phenomenon.

Methods and results: In the data of our stress testing in hypertension study, 131 hypertensives with chest pain symptom were assessed by exercise electrocardiographic test (EET), exercise myocardial scintigraphy with 99 m-technetium sestamibi (MIBI-SPECT) and by dobutamine echo (DE) before coronary angiography. From 61 consecutive patients with no significant CAD, 38 (62%) met criteria for positive results at least in one test, which occurred mostly in women (82%, $P < 0.001$). The false positive response was 29 to EET, 28 to MIBI scan and 13 to DE, with a specificity of 53%, 54% and 80% ($P < 0.01$, vs both MIBI and EET), respectively. This figure related to a lower specificity of EET in patients with either resting ST-T abnormalities or left ventricular hypertrophy (LVH) than in the remainder (33% vs 89%, $P < 0.01$) and a lower MIBI scan specificity only in patients with LVH (31% vs 66%). DE tended to have a lower specificity in patients with than without LVH (69% vs 88%, P =NS). The false-positive responses of any tests were not attributable to rest regional dysfunction and rest myocardial perfusion defect.

Conclusions: our findings limit the applicability of EET and MIBI scan in unselected hypertensive patients: the former is not valid in patients with either rest ST-T changes or LVH and the latter is limited in patients with LVH. In such group, the use of DE has the potential to avoid unnecessary invasive procedures.

Keywords: Hypertension; Exercise testing; Stress echocardiography; Coronary artery disease

PO-187

INADEQUATE BLOOD PRESSURE CONTROL IN HYPERTENSIVES REFERRED FOR CARDIAC STRESS TESTING

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Background: Hypertension (HTN) is the most common primary diagnosis in the US, affecting approximately 30% of the adult population. Hypertensive patients are at increased risk for cardiovascular disease (CVD). Achieving adequate BP control can reduce morbidity and mortality from CVD. We sought to examine the degree of BP control in hypertensive patients referred for cardiac stress testing. Additionally, we hypothesized that patients with poor BP control would have a higher incidence of ischemia on perfusion imaging.

Methods: We retrospectively analyzed 2,039 patients with the diagnosis of hypertension referred to our nuclear cardiology laboratory for stress testing from January 2007 through July 2010. Patient's resting blood pressure was categorized as follows: controlled (<140/90), poorly controlled (140–160/90–100), very poorly controlled (>160/100). The incidence of ischemia was defined as the presence of a reversible perfusion defect on stress/rest single photon emission computed tomography (SPECT) scan.

Results: Patients had a mean age of 68 ± 13 years, 885 (43.4%) were males, 742 (36.4%) had diabetes, 1189 (58.3%) had dyslipidemia, and 767 (37.6%) had history of coronary heart disease (CHD). The results are summarized in the following table:

Conclusion: We found that over half of patients referred for stress testing had uncontrolled hypertension, and almost one quarter had a BP >160/100. This represents suboptimal treatment in a group of co-morbid patients with suspected or known CHD. Additionally, in contrast to our hypothesis, patients with the poorest BP control had a lower incidence of ischemia compared to those patients with relatively better BP control. One possible explanation for this finding is that those with very poorly controlled BP may be experiencing symptoms mimicking ischemic heart disease but rather caused by their markedly elevated BP. Quality of care might be improved by optimally controlling BP prior to ordering diagnostic testing associated with radiation exposure and cost.

	Number (%)	Presence of ischemia; n (%)	*P* value
Controlled HTN	962 (47.2)	191 (19.8)	
Poorly controlled HTN	602 (29.5)	116 (19.3)	†NS
Very poorly controlled HTN	475 (23.3)	68 (14.3)	*<0.05

†Incidence of presence of ischemia compared to controlled HTN group
*Incidence of presence of ischemia compared to controlled HTN and poorly controlled HTN groups

Keywords: Coronary artery disease; Poor hypertension control; Nuclear stress testing

PO-188

RELATIONSHIP BETWEEN EXERCISE INTOLERANCE AND PLASMA NATRIURETIC PEPTIDE LEVEL IN HYPERTENSIVES WITH POSTINFARCTION CARDIOSCLEROSIS

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Background: N-terminal pro–brain natriuretic peptide (NT-pro BNP) is an established biomarker for heart failure (HF).The aim of the investigation was to determine interconnection between plasma NT-pro BNP levels and causes of exercise intolerance in hypertensives with postinfarction cardiosclerosis.

Methods: This study included 29 hypertensives (men, age $\geq$55 years) diagnosed with HF in NYHA class I-II and preserved left ventricular ejection fraction (LVEF>50%) after 1.5–2 years follow-up of myocardial infarction. All patients were divided into 3 groups accordingly to the plasma NT-pro BNP levels: 8 patients with NT-pro BNP levels <100 pg/mL (group I); 12 patients with NT-pro BNP levels in the range 100–200 pg/mL (group II); nine patients with NT-pro BNP levels >200 pg/mL (group III). Blood pressure (BP), echocardiography, upright bicycle ergometer, plasma NT-pro BNP levels by ELISA methods were measured. The control group consisted of 10 healthy people.

Results: The basal plasma NT-pro BNP levels were equal to (62.33 ± 5.24) pg/mL (group I) ($P > 0.05$); (134.55 ± 10.89) pg/mL (group II) ($P < 0.05$) and (281.33 ± 13.64) pg/mL (group III) vs (55.30 ± 5.33) pg/mL in the control group ($P < 0.05$). The main reasons of stoppage exercise were dyspnea in 2 (25.00%) cases or angina pectoris in 6 (75.00%) cases (group I); dyspnea with angina pectoris in 11 (91.67%) cases (group II); dyspnea with angina pectoris in 6 (66.67%) cases (group III) accordingly. ST segment depression >2 mm was in 1 (8.33%) case (group II) and in 1 (11.11%) case (group III); systolic BP decreased by >20 mmHg in 2 (22.22%) cases (group III). The time of HR recovery was 5 min in 6 (75.00%) and 7 min in 2 (25.00%) cases (group I); 5 min in 3 (25.00%) and 7 min in 6 (50.00%) and 9 min in 3 (25.00%) cases (group II); 7 min in 5 (55.56%) and 9 min in 4 (44.44%) cases (group III). In patients with plasma NT-pro BNP levels over 200 pg/mL the time of HR recovery was significantly greater than in patients with the normal plasma NT-pro BNP levels.

Conclusions: It is suggested that exercise intolerance with early appearance of angina pectoris, dyspnea and ST segment depression >2 mm is associated with impaired HR recovery after cessation of exercise and with increasing of plasma NT-pro BNP levels.

Keywords: Natriuretic peptide; Exercise intolerance

PO-189

INFLUENCE OF A HISTORY OF HYPERTENSION WITH CLINICAL PRESENTATION AND PROGNOSIS AFTER ADMISSION WITH NON ST SEGMENT ELEVATION ACUTE CORONARY SYNDROME

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Background and objective: Chronic hypertension (HTN) is a well established risk factor for the development of cardiovascular disease; however, its prognostic significance after a non-ST-segment elevation acute coronary syndrome (NSTE-ACS) remains to be established. The aim of our study was to determinate if hypertensive patients differ from non-hypertensives in the epidemiological profile, clinical presentation and hospital and long term prognosis after NSTE-ACS.

Patients and methods: We prospectively included 415 patients with NSTE-ACS and looked for the combined end-point of cardiac death or myocardial infarction at long- term (mean follow-up 50 months). Prognostic variables were determined during admission. For group comparisons we used Student's *t*-test and χ^2 test. Values of $P < 0.05$ were considered significant. Survival analyses were performed with a Kaplan-Meier (univariate) and Cox regression (multivariate) tests.

Results: A history of hypertension was present in 204 (49%). Patients with HTN were older (67 vs 60 years, $P < 0.0001$), and more likely to be female (38% vs 18%, $P < 0.0001$). Patients with HTN were also more likely to have diabetes mellitus, peripheral vascular disease, prior history of heart failure and atrial fibrilation but less likely to be cigarette smokers. At admission, HTN patients had higher Killip class, heart rate, inflammatory marker levels and ECG-changes. There were no differences in hospital mortality-myocardial infaction between these groups, 5.4% vs 3.8% (OR = 1.4, 95% CI 0.6–3.7, $P = 0.43$). An event-free survival was observed in 83% of patients without HTN but only in 73.5% of those with HTN, $P < 0.01$. The multivariate analysis showed that cronic hypertension was an independent predictor of adverse events in the follow-up: 1.9, 95% CI 1.17–3, $P < 0.01$.

Conclusion: Although Hypertensive patients displayed a worse epidemiological, electrocardiographic and biochemical profile, they havent worse in-hospital outcome than normotensive patients. However, chronic hypertension remains an independent marker for major long-term cardiac adverse outcomes after non-ST-segment elevation acute coronary syndrome.

Keywords: Hypertension; Acute syndrome coronary; Prognosis; Heart diseases

PO-190

CHARACTERISTICS OF HYPERTENSIVE RESPONSE DURING EXERCISE ECHOCARDIOGRAPHY IN HYPERTENSIVE PATIENTS WITH NO HISTORY OF CORONARY ARTERY DISEASE

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A hypertensive response has been shown to cause false-positive exercise electrocardiographic test results. Exercise echocardiography (Ex-echo) has superior accuracy over exercise electrocardiography. We were to assess the characteristics of hypertensive response during Ex-echo in patients with hypertension compared to normotensive subjects.

Of 154 patients, with no history of coronary artery disease (CAD), who had coronary angiography (CAG) within four weeks after treadmill Ex-echo, 89 were hypertensive patients and 65 were normotensives. A hypertensive response to exercise was defined as systolic blood pressure (SBP) > 220 mmHg for men and SBP >190 mmHg for women or diastolic blood pressure (DBP) > 90 mmHg during Ex-echo.

Ex-echo showed higher specificity (88% vs 67%) and good positive predictive value (90% vs 75%), but lower sensitivity (66% vs 71%) for predicting significant CAD on CAG in patients with

hypertension than normotensives. Although the hypertensives showed higher prevalence of hypertensive response in SBP than normotensives (18% vs 5%, $P = 0.01$), the prevalence of hypertensive response in DBP, significant CAD on CAG and the positivity on Ex-echo were not different between the group.
In conclusion, Ex-echo showed higher specificity for predicting CAD in the hypertensives who showed a higher hypertensive response in SBP than the normotensives, but similar prevalence of CAD on CAG and positivity on Ex-echo compared to the normotensives. In patients with hypertension with no history of CAD, a hypertensive response to exercise does not seem to affect the false positive result of Ex-echo.

Keywords: Hypertensive response; Exercise test

PO-191

THE ANKLE-BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE

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The ankle-brachial index (ABI) also presents information about general CV health. The objective of this study was to examine the relation between ABI and the extent of coronary atherosclerosis in a cohort study of patients who had coronary heart disease (CHD) and also, they had coronary angiography performed. Methods: 100 consecutive patients have been studied (45 women, mean age 59.7 ± 10 years) who had CHD and who also had coronary angiography performed, ABI evaluation, ultrasound imaging for intima-media thickness measurement of carotid arteries, and SCORE risk were evaluated. Results: Average SCORE risk of our patients was 6.6 ± 5. Regarding the vascular risk factors tested in multiple regression analysis, only SCORE risk ($P = 0.003$) was related independently to ABI. The value of ABI in patients of average value 1.02 ± 0.21. In the experimental group 41 (41.0%) patients had reduced ABI value (<0.9), and 18 (18.0%) of them had higher values (>1.3). The extent of the coronary artery disease was marked as 0–3 according to the number of the coronary vessels with narrowing. In most patients, 42 (42.0%) had stenosis marked greater than 70% in one coronary vessel; 34 (34.0%) had narrowing in two vessels; and in 18 pts (18.0%) narrowing was in three vessels, while in 6 (6.0%) narrowing was not diagnosed in any coronary vessel. The value of the ABI in patients with three affected coronary vessels, atherosclerosis was the lowest (0.95 ± 0.18) and significantly lower than in those with only one affected coronary vessel (1.12 ± 0.20, ANOVA and Tukey test: $P < 0.01$). When the multivariate regression analysis implement the influence of age, gender, hyperlipoproteinemia and diabetes mellitus, important factors associated with the number of affected coronary atherosclerotic blood vessels are ABI values, the thickness of intima media and relations waist/hip. Each rise of ABI value only in one unit, blood vessel is affected by decrease of 0.823 (95% IP: 0.149, $P < 0.05$). Multivariate analyses of variance showed statistically significant effects of individual values of ABI index ($F = 2.71$: $P < 0.05$), number of plaques in carotid arteries ($F = 2.18$: $P < 0.05$), almost SCORE risk ($F = 4.39$: $P < 0.001$) and age ($F = 3.14$: $P < 0.01$) according to values of the stenosis percentage in individual coronary arteries.

Conclusion: ABI index related to the extent of generalized atherosclerosis in coronary arterial beds, suggests generalized atherosclerosis.

KeywordsAnkle-brachial index; Hypertension; Coronary heart disease

Genetics/Gene Therapy/Proteomics

PO-192

CARDIAC BNP GENE DELIVERY PREVENTS HYPERTENSIVE HEART DISEASE IN SPONTANEOUS HYPERTENSIVE RATS

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Background: Diastolic dysfunction associated with high blood pressure (BP) leads to cardiac remodeling and fibrosis and progression to congestive heart failure. B-type natriuretic peptide (BNP) has BP lowering, anti-fibrotic and anti-hypertrophic properties, which makes BNP an attractive agent for attenuating the adverse cardiac remodeling associated with hypertension. In the current study, we tested the effects of sustained cardiac proBNP gene delivery on BP, cardiac function and remodeling in spontaneous hypertensive rats (SHR).

Methods and Results: We used the myocardium-tropic adeno-associated virus serotype 9 (AAV9) vector to achieve continuous cardiac rat proBNP expression. In SHR single systemic administration of AAV9 vector allowed long-term, cardiac BNP overexpression, resulting in significant reductions in systolic and diastolic BP for nine months after injection. Left ventricular (LV) thickness, LV end-systolic dimensions and LV mass were reduced, while ejection fraction was significantly increased in BNP-treated compared to untreated SHR. Circumferential systolic strain and strain rate of the early phase of diastole were improved in BNP-treated compared to untreated SHR. Importantly, non-cardiac overexpression of BNP via AAV2 vector was not associated with changes in BP and plasma BNP in SHR. Furthermore, normal Wistar rats injected with AAV9 proBNP vector showed significantly reduced heart weights four weeks after injection without BP reduction.

Conclusions: AAV9 vector facilitates sustained cardiac proBNP overexpression, which reduces BP and improves LV function in hypertensive heart disease. Long-term proBNP delivery improved both systolic and diastolic function. Importantly, the effects on cardiac structure and function occurred independently of BP lowering effects in normal Wistar rats.

Keywords: Natriuretic peptides; Cardiac structure and function; Gene delivery

PO-193

DNA VARIANTS IN NOS3 ARE ASSOCIATED WITH IMPROVED SMALL ARTERY ELASTICITY AND DECREASED SYSTOLIC BLOOD PRESSURE

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Background: Small artery elasticity is a functional marker, which predicts the onset of arterial hypertension in normotensive subjects. The Multi-Ethnic Study of Atherosclerosis showed that small artery elasticity has also a predictive value for cardiovascular morbidity and mortality in subjects free of overt cardiovascular disease (CVD). Small artery elasticity reflects endothelial (dys)function.

Objective: to determine if small artery elasticity and systolic blood pressure were associated with DNA variants in NOS3.

Methods: A total of 536 subjects (356 males, 180 females) free of overt CVD, who attended the primary CVD prevention clinic were enrolled in the study. Large and small artery elasticity were derived from the diastolic pulse contour analysis of the radial artery waveform using non-invasive arterial tonometry. Systolic blood pressure (SBP) was measured in sitting position using an automatic blood pressure device. 9 tagged SNPs in NOS3 were genotyped using mass spectrometry (Sequenom), with a call rate > 99.5%. Logistical regression analysis was carried out in PLINK. Genotype distributions were in accordance with Hardy-Weinberg equilibrium expectations. Covariates included age, race, and sex.

Results: SNP rs3730006 was associated with lower SBP (G/G, 129 ± 17 mmHg n = 494, A/G, 125 ± 14 mmHg, n = 24, and A/A, 114 ± 6 mmHg, n = 2; $P < 0.05$), and marginally associated with improved small artery elasticity (G/G 6.5 ± 3.2 mL/mmHgx100, n = 493, A/G, 6.9 ± 3.8 mL/mmHgx100, n = 24, and A/A, 9.95 ± 3.75 mL/mmHg, n = 2; $P < 0.06$). In addition, a significant association was found in a haplotype block including two SNPs rs1799983 (Glu298Asp) and rs3918227 and decreased SBP ($P < 0.05$).

Conclusions: These novel findings suggest that DNA variants in NOS3 are associated with improved small artery elasticity and decreased systolic blood pressure.

Keywords: Arterial elasticity; Systolic blood pressure; NOS3

PO-194

SNP-SNP INTERACTIONS AMONG HYPERTENSION RELATED GENES

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Objective: Essential hypertension (HT) is considered to be the result of the interactions of many genes and environmental factors. Although case-control studies can provide a powerful approach for detecting single nucleotide polymorphisms(SNPs), few studies have considered their interaction.The aim of this study was to evaluate interactions between genes by comparing the effects of SNP alone with the joint effects of two SNPs.

Methods: We investigated four SNPs of Paraoxonase1(PON1),Uncoupling protein2(UCP2), Angiotensinogen(AGT) and Resistin(RETN) in a case-control study. Recruited were 189 HT patients and 245 controls in Japan. Genotyping was done in Jichi Medical University.The effects of each SNP alone and combinations of two SNPs on HT were analyzed by using logistic regression models. The strength of the associations was estimated by odds ratios(ORs). The OR of SNP alone was calculated by using homozygous non-risk genotype as reference. To assess joint ORs for the 2 genotypes combined, we subdivided the data into 9 strata according to the cross-classified genotypes. We then obtained the ORs for each of the strata relative to the first stratum defined by non-risk genotype for both genes.

Results: The ORs of the homozygous risk genotype for PON1 was 3.75(95%CI 1.74–8.10) and for UCP2 was 1.85(1.01–3.40), while the joint OR of highest-risk genotype (presence of homozygous risk alleles for both genes) was 7.94(1.60–39.4). The OR of the homozygous risk genotype for AGT was 2.22(0.62–7.95) and the joint OR of highest-risk genotype for PON1 × AGT was 24.8(2.56–241). The OR of the homozygous risk genotype for RETN was 1.56(0.80–3.06) and the joint OR of highest-risk genotype for PON1 × RETN was 5.97(1.05–33.8).

Conclusions: SNP-SNP interactions between PON1 and AGT may lead to higher risk on hypertension in Japanese population.

Keywords: SNP; Interaction; Essential hypertension; Japanese

PO-195

BLOOD PRESSURE, ENDOTHELIAL DYSFUNCTION, LIPID PROFILE AND CYP3A5 GENE POLYMORPHISM IN UZBEK HYPERTENSIVE PATIENTS

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Aim: To study of systemic hemodynamics, vascular remodeling, and lipid profile features in Uzbek hypertensive patients in association with A6986G polymorphism of CYP3A5 gene.

Methods and Material: Study included 80 Uzbek men with I–II grade of AH in the mean age of 44.97 ± 9.50. Physical examination, "office" blood pressure measurement, test with reactive hyperemia, estimation of carotid intima-media thickness (CIMT), blood lipid level assessment and genotyping on A6986G polymorphism of CYP3A5 gene were performed.

Results: Twenty-three (28.75%) of patients have *1/*3 heterozygous genotype, and 57 (71.25%) – have *3/*3 homozygous genotype (χ^2 = 28.90; P = 0.000). There were no patients with *1/*1 homozygous genotype observed. Patients also subsequently were divided into groups with *1/*3 and *3/*3 genotypes carriage. SBP in patients with *1/*3 genotype was 164.71 ± 11.25 vs 149.77 ± 9.13 mm Hg in patients with *3/*3 genotype (P = 0.000). DBP was 105.00 ± 8.66 vs 97.33 ± 5.60 mm Hg (P = 0.000). Values of HR, ΔD, CIMT as well as blood lipid profile indicators revealed no significant differences associated with carriage of the studied genotypes and alleles. Thus, in carriers of *1/*3 genotype HR was 82.41 ± 5.81 bpm, while the carriers *3/*3 genotype – 82.26 ± 5.89 bpm (P = 0.926). The values of ΔD in carriers of *1/*3 genotype were 2.11 ± 4.71% vs 4.50 ± 4.32% in patients with *3/*3 genotype (P = 0.065). CIMT in patients with carriage of *1/*3 genotype was 1.00 ± 0.17 vs 0.94 ± 0.16 mm in carriers of *3/*3 genotype (P = 0.232). In patients with *1/*3 and *3/*3 genotypes, TC level was 199.82 ± 46.51 vs 190.67 ± 28.86 mg/dL (P = 0.360); TG – 154.00 ± 59.33 vs 158.28 ± 55.36 mg/dL (P = 0.792); HDL-C – 41.65 ± 8.29 vs 40.56 ± 5.69 mg/dL (P = 0.562), LDL-C – 127.82 ± 38.26 vs 119.21 ± 27.55 mg/dL (P = 0.334).

Conclusion: Obtained results suggest that carriage of *1/*3 genotype of A6986G polymorphism of CYP3A5 gene are associated with a higher blood pressure level in Uzbek hypertensive men, having no significant association with heart rate, indicators of vascular remodeling and blood lipid profile.

Keywords: Arterial hypertension; Endothelial dysfunction; Genetic polymorphism; CYP3A5

PO-196

MITOCHONDRIAL POLYMORPHISMS ARE ASSOCIATED WITH BLOOD PRESSURE AND METABOLIC TRAITS IN THE FRAMINGHAM HEART STUDY

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Background: Hypertension (HTN) is a major risk factor for myocardial infarction, heart failure, and stroke. To date, only very limited insights into HTN have come from research on the mitochondrial genome, which encodes elments that play key roles in oxidative phosphorylation, a converging point of major metabolic pathways. Our goal was to identify mitochondrial single nucleotide polymorphism (mtSNP) influencing the blood pressure (BP) and metabolic phenotypes.

Methods: Novel variants were identified through sequencing of the entire mitochondrial genome from 38 individuals with extreme BP defined as the sum of the residuals (adjusted for age, sex, and BMI) for systolic and diastolic BP fell in the top or bottom 1%. MtSNPs were selected if they were: non-synonymous, or involved in regulation of mitochondrial function, or used to categorize European mitochondrial lineage. Forty mtSNPs were genotyped on ~7000 Framingham Heart Study (FHS) participants. The association analysis was performed using a linear mixed effects (LME) or generalized equation estimation equaling (GEE) model, respectively, for continuous or binary phenotypes.

Results: Association analyses and permutation tests identified mutations that were related to BP/HTN (four mtSNPs); fasting blood glucose (FBG)/diabetes (five mtSNPs); and body mass index (BMI)/obesity (three mtSNPs). Among these identified loci, a non-synonymous rare variant (minor allele frequency = 0.006) in cytochrome C oxidase subunit, displayed statistically significant associations across multiple BP (for HTN, OR = 4, empirical *P*-value = 0.0062) and FBG phenotypes (for diabetes, OR = 5, empirical *P*-value = 0.003).

Conclusions: We have identified novel mtSNPs that might be related to BP and metabolic phenotypes. These novel variants warrant further functional studies. *Drs. Schwartz and Levy contributed equally to the work.

Keywords: Hypertension; Mitochondrial single nucleotide polymorphism; Maternal lineage; Metabolic traits

PO-197

HAPTOGLOBIN POLYMORPHISM IN WOMEN WITH PREECLAMPSIA IN ISRAEL

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Preeclampsia is a leading cause of maternal morbidity and mortality. Many etiologies have been implicated in its pathogenesis. One hypothesis postulates a causative role of oxidative stress-oxygen radicals. Antioxidants, might have a protective effect in preeclampsia. Haptoglobin (Hp) is a hemoglobin-binding plasma protein, and has antioxidant properties due to chelating oxidative heme groups. Hp has three genotypes, producing the phenotypes 1-1, 1-2 and 2-2. Hp1-1 is allegedly a more potent antioxidant due to its smaller size.

Objective: To determine whether Hp1-1 was less common in women with preeclampsia which is a disease with an oxidative-stress component, compared to the healthy population.

Methods: Haptoglobin phenotype was compared in 240 healthy and 120 preeclamptic gravida (matched by origin: jewish/arabs), delivered at the Bnai-Zion Medical Center. Preeclampsia was defined as blood pressure exceeding 140/90 in repeat measurements, together with proteinuria of +1 or more in dipstick or 300 mg or more in 24 hour urine collection. Blood was collected upon arrival to the delivery room or maternity ward, centrifuged and frozen until analyzed.

Results: Two hundred and forty healthy women and 120 women with preeclampsia were included in this study. Among women with preeclampsia, seven had the Hp1-1 phenotype, 62 had the Hp2-1 phenotype, and 51 had the Hp 2-2 phenotype. In the control group, 30 women had the Hp 1-1 phenotype, 109 had the Hp 2-1 phenotype and 101 had the Hp 2-2 phenotype. The difference between the Hp 1-1 phenotype vs non 1-1 phenotype prevalence in the two groups (e.g. preeclampsia and healthy) was statistically significant, with a $P > 0.05$. Among women with the Hp 1-1 phenotype, 7/37 (18.9%) had preeclampsia and 30/37 (81.1%) were healthy, in women with the 2-2 phenotype, 51/152 (33.6%) had preeclampsia and 101/152 (66.4%) were healthy, and in women with the Hp 2-1 phenotype, 62/171 (36.3%) had preeclampsia and 109/171 (63.7%) were healthy.

Conclusions: The prevalence of haptoglobin 1-1 is higher in healthy, compared to preeclamptic gravidas. This finding is compatible with a protective role of Haptoglobin 1-1, in the pathogesesis of preeclampsia, possibly through its antioxidative properties. Haptoglobin phenotype may be one component in a set of additional markers that may be used as an early screening tool for the future development of preeclampsia.

Keywords: Haptoglobin; Arterial hypertension; Preeclampsia; Proteinuria

PO-198

TARGETED DISRUPTION OF *NPR1* GENE UPREGULATES RENIN-ANGIOTENSIN SYSTEM AND CARDIAC HYPERTROPHY IN NULL MUTANT MICE

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Atrial and brain natriuretic peptides (ANP and BNP) bind guanylyl cyclase-A/natriuretic peptide receptor-A (GC-A/NPRA) and produce intracellular second messenger cGMP. The objective of the present study was to examine whether disruption of *Npr1* gene (coding for GC-A/NPRA) initiates the activation of the renin-angiotensin system (RAS). Genetic disruption of *Npr1* gene increases 35–40 mm Hg systolic blood pressure and 63% greater heart weight/body weight (HW/BW) ratio leading to congestive heart failure in null mutant ($Npr1^{-/-}$) mice compared with wild-type ($Npr1^{+/+}$) mice. The expression levels of angiotensin-converting enzyme (ACE) and angiotensin II type 1a receptor (AT1a) mRNA levels were increased by fourfold and fivefold, respectively, in $Npr1^{-/-}$ mice hearts compared with wild-type mice. The expression of interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and transforming growth factor-beta1 (TGF-β1) were increased by 4- to fivefold, in null mutant mice hearts compared with wild-type counterparts. The nuclear factor-kappa B (NF-κB)

binding activity and its expression was increased by fourfold and fivefold, respectively, in the nuclear extracts of *Npr1*$^{-/-}$ mice hearts compared with wild-type mice. Treatment with captopril, hydralazine, and bendrofluomethiazide equally reduced the blood pressure, but only captopril significantly decreased the HW/BW ratio and expression of Il-6, TNF-α, and TGF-β1 in *Npr1*$^{-/-}$ null mice hearts. The data indicate that the disruption of ANP/NPRA signaling leads to the enhanced expression of RAS-mediated signaling pathways that provoke pro-inflammatory cytokines and promote the development of cardiac hypertrophy, fibrosis, and congestive heart failure in null mutant mice.

Keywords: Atrial natriuretic peptide; Renin-angiotensin system; Gene disruption; Cadiac hypertrophy

Heart Failure/Hypertrophy (Diastolic Dysfunction)

PO-199

A META-ANALYSIS OF THE EFFECT OF ANTI-HYPERTENSIVE TREATMENT ON ECHOCARDIOGRAM PARAMETERS IN HEART FAILURE PATIENTS WITH PRESERVED EJECTION FRACTION

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Background: We sought to investigate the effects of ACE inhibitors (ACE-I) angiotensin receptor blockers (ARB), β-blockers (BB) and calcium channel blockers (CCB) on the echocardiographic parameters in heart failure patients with preserved ejection fraction (HF-PEF).

Methods: MEDLINE was searched for longitudinal studies using two-dimensional and Doppler echocardiography for quantification of LV function at baseline and at follow-up. Primary endpoints were the change in the integrated quantitative assessment of mitral flow E:A ratio, deceleration time (DT), and isovolumic relaxation time (IVRT). Treatment arms of the same drug class, weighted for the number of patients, were combined. The unpaired Student *t* test was used to compare the change in these parameters as compared to baseline. Publication bias was assessed by examining funnel plot.

	E/A	IVRT	DT
RAAS inhibitors	Basal: 0.895 (± 0.126) F/U: 0.964 (± 0.109) p < 0.0001*, n = 790	Basal: 101.2 (±11.8) F/U: 97.5 (±10.6) p < 0.0001*, n = 447	Basal: 221.3 (± 16.1) F/U: 214.2 (± 20.0) p < 0.0001*, n = 447
ACE	Basal: 0.826 (± 0.081) F/U: 0.905 (± 0.102) p < 0.0001*, n = 397	Basal: 96.1 (± 15.9) F/U: 91.4 (±12.5) p = 0.008*, n = 131	Basal: 208.5 (±9.9) F/U: 187.7 (±14.7) p < 0.0001*, n = 131
ARB	Basal: 0.964 (± 0.126) FU: 1.024 (± 0.082) p < 0.0001*, n = 393	Basal: 103.4 (± 8.7) FU: 100.0 (± 8.5) p < 0.0001*, n = 316	Basal: 226.6 (±15.3) FU: 225.2 (±8.1) p = 0.151, n = 316
BB	Basal: 0.860 (± 0.099) FU: 0.952 (± 0.114) p < 0.0001*, n = 189	Basal: 93.8 (±14.4) FU: 94.6 (±14.5) p = 0.65, n = 136	Basal: 211.8 (±16.9) FU: 220.3 (±16.9) p < 0.0001*, n = 163
CCB	Basal: 0.787 (± 0.099) FU: 0.798 (± 0.094) p = 0.19, n = 267	Basal: 106 (+/- 17) FU: 103 (+/- 5.9) p = 0.32, n = 35	Basal: 226.9 (±28.4) FU: 209.6 (±39.5) p = 0.01* , n = 50

Values expressed as : Mean (+ SD), n = number of patients
* - change in follow up value is statistically significant at p < 0.05

Results: A total of 18 studies with 26 arms, examining data from 1206 participants met our inclusion criteria and were included in the final analysis. RAAS inhibitors as a group and the subgroup of ACE-I showed a consistent statistically significant improvement of all the three examined parameters, i.e. E:A, IVRT and DT. For the ARB subgroup, although all the three parameters improved, the improvement in DT did not reach statistical significance. The BB results showed a statistically significant improvement of E/A, but the IVRT and DT parameters did not improve. Similarly with CCB's, although there was a change in DT, there were no changes in E/A and IVRT (Figure 1).

Conclusion: Antihypertensive drug classes appear to have different effects on echocardiographic parameters associated with DD, with the RAAS inhibitors showing a greater benefit compared to CCB and BB. Whether an improvement in the echocardiogram parameters translate into better clinical outcomes remains to be determined.

Keywords: Diastolic dysfunction; ACE inhibitors; E:A ratio

PO-200

EFFECTS OF RENIN-ANGIOTENSIN SYSTEM BLOCKADE ON MORTALITY AND REHOSPITALIZATION IN HEART FAILURE WITH PRESERVED EJECTION FRACTION

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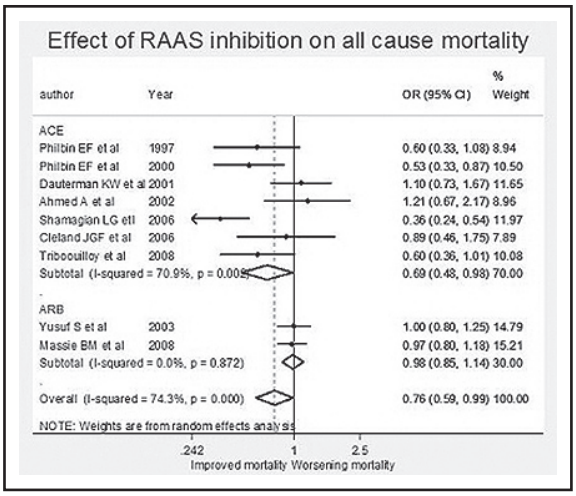
Background: Heart Failure with Preserved Ejection Fraction (HF-PEF) is a well recognized complication of long standing hypertension. However, beyond the control of the traditional cardiovascular risk factors, there are few other recommendations for its management. To examine the potential benefit of renin-angiotensin system (RAAS) inhibition in HF-PEF, we performed a systematic review of the published medical literature.

Methods: MEDLINE database was searched from 1966 to November 2010 for longitudinal studies examining HF-PEF patients receiving treatment with RAAS inhibitors, either ACE inhibitors (ACE-I) or Angiotensin Receptor Blockers (ARB) in addition to their standard treatment compared to those receiving standard treatment alone. We examined two major outcomes: all-cause mortality and rehospitalizations for heart failure. DerSimonian and Laird estimate for random-effects model was used for between studies variance. Small study bias was examined using the funnel plot.

Results: A total of nine studies with 10,224 participants were included in the analysis. As compared to the standard group, RAAS inhibition group exhibited a statistically significantly lower odds of all-cause mortality (OR 0.76, 95% CI 0.59–0.99). In subgroup analysis, seven studies on ACE-I showed a decrease in the odds for all-cause mortality (OR 0.69, 95% CI 0.48–0.98, Figure 1). In a total of seven studies with 9746 participants, RAAS inhibition showed a trend towards lowering the odds of rehospitalization (OR 0.9, 95% CI 0.77–1.05). In the subgroup analysis, five studies on ACE-I also showed a similar trend (OR 0.88, 95% CI 0.65–1.19).

Conclusion: RAAS inhibition in HF-PEF is associated with a small but consistent reduction in the all-cause mortality, with a trend towards lower odds of rehospitalization. Further prospective randomized trials are warranted to confirm the effects of RAAS inhibition on mortality and rehospitalization (Figure 1).



Keywords: Diastolic dysfunction; RAAS inhibition

PO-201

SOCIOECONOMIC STATUS AND COSTS IN HEART FAILURE

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Background: Congestive heart failure is the most common cause for hospital admission in the elderly, affecting >1 million individuals per year with hospital related costs of nearly $18 billion for 2007. Conflicting findings have characterized the association of socioeconomic status (SES), costs and mortality in patients hospitalized with heart failure (HF).

Methods: We conducted a retrospective analysis of the nationwide inpatient sample (NIS) of patients hospitalized with only a primary diagnosis of HF between 2003 and 2005 (n = 3,308,897) to assess the association of patient SES, with length of stay (LOS) and total charges. SES was defined and reported as income quartiles using residential ZIP code characteristics. Associations were evaluated using linear or logistic regression using methods for complex surveys. Model covariates included age, race, gender, primary payer, and 28 of 30 Elixhauser comorbidities. Descriptive analysis showed that the percentage of HF hospitalizations falling into the 1st income quartile was nearly double the percentage falling into the 4th income quartile.

Overall, the mean age was 72.9 years, 52.8% were female, and 28.7% were non-white. Adjusting for age, income quartile 1 (vs quartile 4) showed significantly lower charges and reduced in-hospital mortality. LOS was significantly shorter comparing income quartile 1 vs quartile 2, Q2 vs Q3 and Q2 vs Q4. After adjusting for age, gender, race, insurance and 28 co-morbid variables, income quartile 1 (vs quartile 4) had significantly less charges. Amongst all four quartiles, except for the relationship between quartile 1 and 2, patients with a primary diagnosis of heart failure had an independent, strong, consistent and graded relationship between socioeconomic status and total charges.

Conclusions: A primary diagnosis of heart failure among inpatients and its strong graded relationship between SES and total charges creates opportunities for intervention during the current economic downturn.

Table I. Percentage of primary CHF vs ALL other hospitalizations

Income quartiles	CHF % (SE)	All others % (SE)
1st	32.62 (0.85)	28.38 (0.74)
2nd	27.01 (0.59)	25.96 (0.51)
3rd	22.50 (0.52)	23.75 (0.43)
4th	17.87 (0.74)	21.92 (0.81)

$P < 0.0001$, P-value based on Chi-Square test (using methods for complex samples)

Keywords: Heart failure; Socioeconomic status; Healthcare costs; Length of stay

PO-202

CAN HIGH DOSE OF VALSARTAN IMPROVE VENTRICULAR-VASCULAR COUPLING IN HEART FAILURE?

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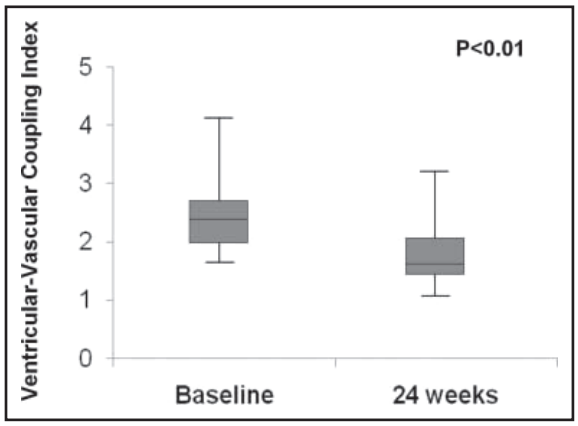
Background: Angiotensin-II type I receptor blockade was supposed to have more beneficial effects on ventricular and vascular function with higher dosage. However, there were few reports about that relationship in heart failure.

Methods: The study participants were forced-titrated to 160 mg of valsartan, bid for 24 weeks. Echocardiography, treadmill test and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were measured at baseline and after 24-weeks therapy.

Results: One hundred thirty-eight patients (59.3 ± 12.4 years old; 66% male; EF; 29.9 ± 5.9%) showed significant improvement in NT-proBNP, left ventricular EF, E/E' ratio and total exercise time in ceiling dose group (n = 72) and non-ceiling one (n = 56), respectively ($P < 0.05$). There were no significant differences in improving LV systolic and diastolic functional parameters between ceiling and non-ceiling dose group. However, ceiling dose group showed much improvements of LV mass index compared with non-ceiling dose group ($P < 0.05$). Interestingly, a significant improvement in the ventricular-vascular coupling



index was observed in the EF <40% of ceiling dose group (from 2.4 ± 0.6 to 1.8 ± 0.5, $P < 0.01$) (Figure 1).

Conclusion: As we expected, valsartan led to a notable improvement in LV systolic and diastolic functions and exercise capacity in patients with heart failure. The ceiling dose of valsartan showed better improvement of ventricular-vascular coupling index in the LVEF < 40% compared with non-ceiling dose group.

Keywords: Ventricular vascular coupling; Valsartan; Heart failure; Angiotensin-II

PO-203

CAN N-TERMINAL PRO-B TYPE NATRIURETIC PEPTIDE PREDICT LV DIASTOLIC DYSFUNCTION IN HYPERTENSIVE HEART DISEASE?

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Background: N-terminal pro-B type natriuretic peptide (NT-proBNP) has been introduced as a useful parameter for assessing left ventricular (LV) systolic function. And left atrial volume index (LAVI) was correlated with chronically elevated LV end diastolic pressure and so reflects LV diastolic dysfunction, which may be important in hypertensive heart disease. However, NT-proBNP about LAVI in hypertensive patients was not yet reported.

Methods: Hypertensive patients whose NT-preBNP and echocardiography were measured within 24 hours were enrolled, but cases with more than 2.0 pg/mL of serum creatinine and acute coronary syndrome were excluded. Finally, 962 patients were analyzed. Data are expressed as means ± standard error of mean or median (25th percentile–75th percentile). NT-preBNP was transformed by the natural logarithm in correlation analysis.

Results: Patients (56.7% female, mean age 64.9 ± 0.4 years) showed moderately decreased LV ejection fraction (EF, 45.5 ± 0.7%) and increased LAVI (40.7 ± 0.9 cc/m^2). NT-proBNP levels ranged from 5 to 35,000 ng/L with a median of 279.4 ng/L (interquatile range, 74–1564 ng/L). NT-proBNP showed significant correlations with EF, LAVI and transmitral E/mitral annular E' ($r = -0.540$ and $P = 0.000$, $r = 0.546$ and $P = 0.000$ and $r = 0.463$ and $P = 0.000$, respectively). And as we expected, NT-proBNP showed significant correlations with LAVI in both the older than 65 years old and the younger ($r = 0.500$ and $P = 0.000$ and $r = 0.574$ and $P = 0.000$, respectively). However, NT-proBNP showed relatively less specific on ROC curve determining LAVI above 27 cc/m^2 (sensitivity 78.2%, specificity: 67.1% at 150 ng/L).

Conclusions: NT-proBNP showed relatively less specific to determe LV diastolic dysfunction. Therefore, NT-proBNP may should be interpreted with combining other clinical information and previous echocardiographic data.

Keywords: Natriuretic peptide; Diastolic dysfunction; Hypertensive heart failure; Left atrial volume index

PO-204

PPARγ AGONIST INHIBITS, AND PPARγ ANTAGONIST EXACERBATES, PRESSURE OVERLOAD-INDUCED CARDIAC FIBROSIS AND DYSFUNCTION

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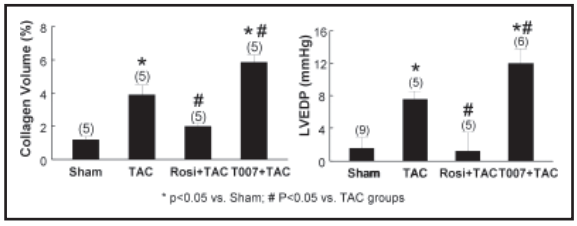
Emerging evidence has indicated that peroxisome proliferator-activated receptorγ (PPARγ) elicits effects on multiple pathophysiologic processes in heart, including left ventricular (LV) hypertrophy and fibrosis, heart failure, and ischemia-reperfusion injury. The current study tested the hypothesis that activation of PPARγ attenuates, and inhibition of PPARγ exacerbates pressure overload-induced cardiac fibrosis and dysfunction in mice. Male C57BL6 mice were subjected to transverse aortic constriction (TAC) or sham surgery and treated with the PPARγ agonist rosiglitazone (Rosi, 10 mg/kg), the PPARγ antagonist T0070907 (T007, 1.5 mg/kg), or vehicle by gavage daily beginning 3 days and continued for 3 weeks after TAC. LV end-diastolic pressure (LVEDP) was measured as an index of cardiac function and interstitial collagen deposition was measured (by picrosirius red staining) as an index of cardiac fibrosis. Rosiglitazone significantly attenuated, and T0070907 significantly exacerbated, the TAC-induced increases in myocardial collagen volume and LVEDP. These observations suggest that PPARγ acts as an anti-fibrogenic factor in heart under pressure overload stress in vivo. Maintaining appropriate levels of PPARγ expression/activity in heart is essential for preventing adverse cardiac remodeling and preserving cardiac function under pressure overload stress conditions (Figure 1).



Keywords: PPARgamma; Cardiac fibrosis; Rosiglitazone; PPARgamma antagonist

PO-205

LEFT VENTRICULAR MASS INDEX IS ASSOCIATED WITH COGNITIVE IMPAIRMENT INDEPENDENTLY OF BLOOD PRESSURE IN THE ELDERLY

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Background: Our aim was to deterrmine whether or not the association between cardiac hypertrophy and cognitive impairment is independent of 24-hour blood pressure (BP), particulaly nocturnal BP.

Methods: We recruited 554 ambulatory hypertensive patients who were ≥60 years (mean 74 years; 40%men). They were cross-sectionally examined for 24-hour BP, left ventricular mass index (LVMI), and mini-mental state examination (MMSE).

Results: LVMI was associated with MMSE ($r = -0.340$), both of which were also associated with 24-hour and nocturnal systolic BP (SBP) (all $P < 0.001$). In multiple regression analysis adjusted by significant covariates including 24-hour SBP, pulse pressure, and nocturnal SBP, LVMI was independently associated with MMSE (all $P < 0.001$). When our patients were subdivided into tertiles according to LVMI, those in the highest tertile (mean LVMI: 142.8 ± 14.7, n = 184) had the lowest MMSE scores [geometric mean (SD range); 24.9 (21.7–28.6) vs 26.2 (23.2–29.7) vs 27.2 (24.9–29.8), $P < 0.001$ for linear trend]. This association remained significant even after adjustment for 24-hour and nocturnal SBP (all $P < 0.01$). In multivariate logistic regression analysis, the hazard ratio (HR) (95%CI) for the lowest MMSE tertile (geometric mean MMSE:22.7, n = 180) in the highest vs lower tertiles of LVMI was 2.2 (1.1–3.4); $P < 0.001$.

Conclusion: LVMI was significantly associated with cognitive impairment in elderly hypertensive patients. This association was independent of 24-hour and nocturnal BP.

Keywords: Left ventricular mass index; Cognitive; Hypertrophy; Nocturnal blood pressure

PO-206

HEART FAILURE HOSPITALIZATION IN TENNESSEE (2006–2008): RACE, AGE, AND GENDER ANALYSES

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Purpose: This paper examines heart failure (HF) hospitalization over 3 years (2006–2008) by race, age, gender, and associated risk factors.

Method: Relevant inpatient data on adult patients (aged 20+) from Tennessee Hospital Discharge Data System (HDDS: 2006–2008) were extracted for heart failure (ICD-9 diagnoses of 402, 404, 428) and analyzed by race, gender and seven age categories (20–85+; having 10 year age interval). Prevalence rates were directly age adjusted per 10 K and both crude and adjusted rates ratios were computed (Odds Ratios with 95% Confidence Intervals in logistic models that controlled for HTN, DM, MI, Cholesterol, sex and age).

Findings: The proportion of hospitalized patients (aged 20+) with a primary diagnosis of HF declined from 4.5% in 2006 to 4.2% in 2008. Similarly, HF prevalence rate per 10 K adults (aged 18+) also declined from 43.1 in 2006 to 36.7 in 2008. Despite this overall decline in HF rates, health disparity in HF remained higher for blacks compared to whites. For example, throughout this three-year period, Blacks had higher rates of HF than whites among younger adults aged 20–34 and 35–44 (adjusted B/W rates ratios of nearly 5:1; these B//W ratios tended to decline with increasing age category. Among the younger patients (aged 20–34 and 35–44, HTN was the strongest predictors of HF. Diabetes and MI also emerged as additional strong predictors of HF patients aged 35+.

Conclusion: While the overall rate of HF shows a decline over 3 years, the higher rate of HF among younger black males has remained high at an alarming rate with hypertension and diabetes as major contributory factors. Given the increasing rate of HTN, DM, and Obesity in Tennessee, these findings point to the need of an aggressive and early management of metabolic risk factors to reduce HF health disparity.

Keywords: Heart failure; Health disparity; Race, gender, age

PO-207

REVERSE ASSOCIATION OF EARLY RELAXATION TISSUE DOPPLER WAVES WITH LEFT VENTRICLE MASS IN HYPERTENSIVE NON DIABETIC PATIENTS

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Left ventricular hypertrophy is a major risk factor for cardiovascular mortality. In this study we tried to investigate which of the novel Doppler echocardiographic markers associates more accurately with cardiac mass index in hypertensive non diabetic patients (pts).

One hundred eighty-one consecutive hypertensive pts, 97 men, 84 women, aged 56 ± 9.8 years were compared with 65 non hypertensive controls (38 men, 27 women aged 53 ± 8.7). Pts with diabetes mellitus, coronary artery disease, valvular disease or heart failure were excluded. Our study population underwent echocardiography. Left ventricle (LV) cardiac mass was estimated according to Devereux equation. LV mass index calculated using the body surface area. We also measured: (1) E and A waves from transmitral diastolic flow (2) e and a diastolic and s systolic waves from pulsed wave Tissue Doppler Imaging (TDI) of the mitral annulus at septal ($_s$) and lateral ($_l$) site (3) the flow propagation velocity (VP) from the color M-mode of the diastolic mitral inflow.

Mean LV mass index was 121 ± 35 g/m^2 in hypertensive pts and 104 ± 29 g/m^2 in controls. As presented in the Table I, only e diastolic TDI waves from the septal ($_s$) and the lateral ($_l$) site of mitral annulus are correlated significantly with LV mass index. This association was not found in non hypertensive pts.

Our results show the reverse correlation between early relaxation TDI waves and LV mass index. These TDI diastolic markers seem to be superior in the evaluation of left ventricular hypertrophy in hypertensive non diabetic pts.

Table I.

Echocardiographic markers	E, A, E/A	es	as	E/es	ss	el	al	E/el	sl	VP
LV mass index	NS	$r = -0.23$ ($P = 0.01$) Spearman's correlation	NS	NS	NS	$r = -0.20$ ($P = 0.04$) Spearman's correlation	NS	NS	NS	NS

Keywords: LV mass.

PO-208

ASSOCIATION OF GEOMETRIC PATTERNS OF THE LEFT VENTRICLE WITH MICROALBUMINURIA IN HYPERTENSIVE NON-DIABETIC PATIENTS

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Microalbuminuria in Hypertensive patients (pts) is an important predictor factor for cardiovascular events. In this study we tried to investigate any association between microalbuminuria and the

different geometric patterns of the left ventricle in hypertensive non diabetic patients.

Two hundred and twenty-two consecutive hypertensive pts, 122 men, 100 women, aged 56 ± 9.8 years were examined. Pts with diabetes mellitus, renal deficiency, coronary artery disease, valvular disease or heart failure were excluded. Our study population underwent echocardiograpy. The pts were classified in four types of geometric patterns of the Left ventricle (LV): Normal (NV), concentric remodelling (CR), concentric hypertrophy (CH) and eccentric hypertrophy (EH) according to LV cardiac mass mass index (normal limits <116 g/m^2 for men and <104 g/m^2 for women) and the relative wall thickness (normal limits <0.45). Microalbuminuria was estimated in all pts in a random urine sample as albumine/creatinine ratio.

In our sample 62 pts (28%) had NV, 102 pts (46%) CR, 28 pts (12.5%) CH, and 30 pts (13.5%) EH. The values of albumine creatinine ratio were: 19 ± 15 mg/g in NV group, 30 ± 22 mg/g in CR group, 134 ± 115 mg/g in CH group and 21 ± 10 mg/g in EH group. Only CH type showed significant correlation with microalbuminuria.

Our results show that only the concentric hypertrophy type of the LV correlates significantly with albumine/creatinine ratio in hypertensive non diabetic pts. This type seems to be related more with renal dysfunction than the other geometric patterns of the left ventricle.

Keywords: Left ventricle hypertrophy; Microalbuminuria

PO-209

RELATION OF VENTRICULAR GEOMETRY TO BRAIN NATRIURETIC PEPTIDE LEVELS, EF AND NYHA CLASS IN HEART FAILURE

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Background: Left ventricular (LV) geometry is affected by cardiac remodeling and predicts clinical outcome. Similarly, brain natriuretic peptide (BNP) is elevated in congestive heart failure (CHF) and has prognostic value. However, role of LV geometry in BNP elevation and NYHA function class in patients (pts) presenting with dyspnea is unclear. We investigated relationship of LV geometry with BNP, NYHA class and ejection fraction (EF) in a cohort of pts presenting with dyspnea and suspected CHF.

Methods: We studied 342 consecutive pts (75 ± 13 years, M: F 151:191) admitted with dyspnea to the ER and suspected to have CHF. Pts were divided in two groups [CHF gp (n 200) and Non CHF gp (n 142)] based on symptoms, BNP level (>100 pg/mL) and chest xray. Using echo, Relative Wall Thickness (RWT = 2*post wall thickness/LV diameter) and LV mass index (LVM gm/m^2) LV geometry was divided in 4 gps; normal (RWT < 0.45, LVM < 125), concentric remodeling (RWT ≥ 0.45, LVM < 125), concentric hypertrophy (RWT ≥ 0.45, LVM ≥ 125) and eccentric hypertrophy (RWT < 0.45, LVM ≥ 125).

Results: CHF gp had higher BNP levels (1192 ± 1318 vs 457 ± 787, $P < 0.001$), higher NYHA class (3.3 ± 0.7 vs 2.3 ± 0.6, $P < 0.001$) and lower EF (42 ± 17 vs 53 ± 11, $P < 0.001$). Abnormal ventricular geometry resulted in higher BNP, higher NYHA class and lower EF in CHF gp vs non CHF gp. In both gps, the abnormal geometry tended to produce worse BNP, NYHA or EF scores.

Conclusion: Abnormality of LV mass and wall thickness is common in pts presenting with dyspnea and suspected CHF. Abnormal geometry in CHF pts is associated with worse clinical status compared to non CHF gp.

Keywords: Left ventricular geometry; Congestive heart failure; Brain natriuretic peptide; Ejection fraction

PO-210

THE INFLUENCE OF TELMISARTAN ON PLASMA POTASSIUM LEVELS IN HYPERTENSIVES WITH INSULIN RESISTANCE AND HEART FAILURE

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Background: Blockade of angiotensin AT1 receptors by telmisartan mediates multiple beneficial actions on peripheral insulin responses. The aim of the investigation was to determine the influence of telmisartan on the plasma potassium dynamics in connection with different plasma endogenous insulin (EI) levels in hypertensives with heart failure (HF).

Methods: This study was performed on 45 nondiabetic hypertensives with HF class II–III (NYHA), aged 60 ± 10 years. All patients were divided into three groups depending on plasma EI levels: 23 patients had normal plasma EI levels (group I), 11 patients had reactive hyperinsulinemia (group II), 11 patients had fasting hyperinsulinemia (group III). A control group consisted of 10 healthy people. Methods included daily blood pressure (BP) monitoring, oral glucose-tolerance test with determination of plasma glucose, EI and potassium levels at baseline and after 3 weeks of treatment with including of telmisartan 40–80 mg/day.

Results: Basal and after treatment plasma glucose levels were in the normal range in patients of group I; in groups II and III glucose tolerance was broken. Basal and 2 hour-postloading EI levels were equal to 11.8 ± 4.2 mIU/mL and 13.3 ± 3.2 mIU/mL ($P > 0.05$) (group I); 12.59 ± 3.73 mIU/mL and 27.05 ± 5.91 mIU/mL ($P < 0.05$) (group II); 28.15 ± 5.23 mIU/mL and 29.84 ± 8.6 mIU/mL ($P < 0.05$) (group III) accordingly vs 12.69 ± 3.45 mIU/mL in the control group ($P < 0.05$). Plasma potassium levels were equal to 4.52 ± 0.4 mmol/L (group I)

Table I. Effect of LV geometry on BNP, EF and NYHA class

	CHF group mean ± SD (n)			Non CHF group mean ± SD (n)			Sig α 0.05 P value between CHF and Non CHF group (independent samples test)		
Left ventricular geometry	BNP pg/mL	NYHA class	EF %	BNP pg/mL	NYHA class	EF %	For BNP levels	For NYHA class	For EF %
Normal	810 ± 325 (2)	3.3 ± 0.5 (2)	58 ± 2 (2)	196 ± 146 (9)	2.4 ± 0.5 (10)	61 ± 5 (10)	P 0.17	P 0.03	P 0.86
Concentric remodeling	735 ± 315 (8)	2.9 ± 0.8 (10)	57 ± 8 (10)	221 ± 165 (15)	2.3 ± 0.4 (17)	57 ± 5 (17)	P 0.003	P 0.03	P 0.36
Concentric hypertrophy	971 ± 791 (55)	3.2 ± 0.7 (59)	47 ± 15 (59)	504 ± 753 (52)	2.3 ± 0.5 (54)	53 ± 12 (54)	P 0.009	P < 0.001	P < 0.01
Eccentric hypertrophy	1711 ± 1416 (55)	3.6 ± 0.6 (55)	38 ± 17 (55)	228 ± 215 (50)	2.3 ± 0.5 (53)	50 ± 13 (53)	P < 0.001	P < 0.001	P < 0.001
P value between geometry groups (one way ANOVA)	P 0.003	P 0.01	P 0.07	P 0.02	P 0.80	P < 0.001			

($P > 0.05$); 3.10 ± 0.31 mmol/L in five patients (45%) (group II) and 3.20 ± 0.33 mmol/L in six patients (54.5%) (group III) vs 4.1 ± 0.60 mmol/L in the control group ($P < 0.05$). After treatment plasma potassium levels didn't change in group I vs basal levels ($P > 0.05$). In patients with basal hypokalemia plasma potassium levels increased on 9% and 5% in group II and group III accordingly vs basal levels ($P < 0.05$).

Conclusions: In hypertensives the development of HF is accompanied an increase of hyperinsulinemia degree and in 45–54% cases by the decreasing of plasma potassium levels. Telmisartan promotes the increase of plasma potassium levels in hypertensives with HF and insulin resistance, especially in patients with fasting hyperinsulinemia.

Keywords: Potassium; Insulin resistance; Heart failure; Treatment

PO-211

THE TYPES OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION AND PLASMA NT-PRO BNP LEVELS IN PATIENTS WITH METABOLIC SYNDROME

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Background: The aim of the investigation was to determine interconnection between the types of left ventricular diastolic dysfunction (DD) and plasma NT-pro BNP and endogenous insulin (EI) levels in patients with metabolic syndrome (MS).

Methods: This study included 165 hypertensives (age ≥55 years) diagnosed with heart failure in NYHA class I–II and with sitting systolic blood pressure 150–180 mm Hg. Among them 102 patients had MS by ATP III (2001). All patients were divided into three groups accordingly to the plasma EI levels: 63 patients had normal insulin levels (group I); 64 patients had 2 hour postloading hyperinsulinemia (group II); 38 patients had basal and 2 hour postloading hyperinsulinemia (group III). Blood pressure, oral 2 hour glucose-tolerant tests, plasma EI, NT-pro BNP levels by ELISA methods were measured. Left ventricular diastolic function was evaluated by means of transmitral flow (E, A, E/A ratio, IVRT). The normal diastolic function was determined by E>A, E/A = 1.5, IVRT = 0.063–0.065 ms; DD type 1 by E<A, E/A<1, IVRT > 0.068 ms; DD type 2 by E = A, E/A = 1, IVRT = 0.062–0.063 ms; DD type 3 by E>A, E/A>2, IVRT ≥ 0.067 ms. The control group consisted of 20 healthy people.

Results: The basal plasma NT-pro BNP levels were equal to (166.14 ± 14.09) pg/mL (group I); (180.46 ± 9.83) pg/mL (group II) and (234.79 ± 14.92) pg/mL (group III) vs (107.03 ± 10.20) pg/mL in the control group ($P < 0.05$). The normal diastolic function had 15 patients (23.81%) in group I and four patients (6.25%) in group II and one patient (2.63%) in group III. DD type 1 had 38 patients (60.32%) in group I and 28 patients (43.75%) in group II and 18 patients (47.37%) in group III. DD type 2 had 10 patients (15.87%) in group I and 31 patients (48.44%) in group II and 14 patients (36.84%) in group III. DD type 3 had 1 patient (1.56%) in group II and five patients (13.16%) in group III.

Conclusion: There are correlation association between the plasma NT-pro BNP and insulin levels and unfavourable types of left ventricular DD in hypertensives with MS.

Keywords: Diastolic dysfunction; Natriuretic peptides; Insulin resistance; Metabolic syndrome

PO-212

POSTOPERATIAVE B-TYPE NATRIURETIC PEPTIDE LEVEL ASSOCIATES WITH PROLONGED HOSPITALIZATION AFTER NON-CARDIAC SURGERY IN PATIENTS WITH HYPERTENSION

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Backgrounds: Postoperative cardiovascular complications including death, myocardial infarction, stroke and congestive heart failure, are commonly occurred in patients with hypertension. We evaluated the relationship between postoperative BNP level and postoperative length of stay after non-cardiac surgery in hospital in hypertensive patients.

Patients and Methods: Seventy-three hypertensive patients with orthopedic surgery (mean age 69 ± 13 years, 63 female) were enrolled. Plasma BNP, hemoglobin levels, perioperative intake-output balance at the operation day, the amount of blood transfusion, and clinical data related with cardiovascular complications were collected. Patients with prolonged hospital stay due to operative causes such as wound infection and redo operation were excluded.

Results: There was significant correlation between the length of hospitalization and postoperative BNP level ($r = 0.490$, $P \leq 0.001$). Receiver operating characteristic curves demonstrated postoperative BNP levels as predictors of hospital stay of ≥30 days with areas under the curve of 0.814 (95% Confidence Interval 0.62–1.01). A BNP cut-off value of 83.6 pg/mL had a sensitivity of 87.5% and specificity of 73.5% for predicting postoperative hospital stay of 30 days or more.

Conclusions: It is useful to evaluate the postoperative BNP for predicting the length of hospital stay after non-cardiac surgery in hypertensive patients who have vague, silent and atypical symptoms and signs of congestive heart failure.

Keywords: Natriuretic peptide; Hospitalization; Surgery

PO-213

TREATMENT BLOCKING THE RENIN-ANGIOTENSIN SYSTEM AND 2-YEAR MORTALITY IN VERY OLD PATIENTS WITH HEART FAILURE AND PRESERVED VENTRICULAR EJECTION FRACTION

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Background: Heart failure (HF) with preserved ventricular ejection fraction (PVEF) is the predominant form of HF in the elderly, specially in those with hypertensive cardiopathy. Clinical trials with drugs blocking the renin-angiotensin system have not

shown a clear survival benefit among patients with FH and PVEF. However, the oldest old patients have been under-represented in such trials.

Objective: To assess the effect of the angiotensin converting-enzyme inhibitors (ACEI) and of angiotensin-II receptor blockers (ARB) with mortality over 2 years among very old patients with HF and PVEF.

Methods: Prospective follow-up of patients admitted for acute HF to the geriatrics department of a tertiary hospital from October 2006 to September 2009. The association between treatment with ACEI or ARB and 2-year mortality was summarized with hazards ratios obtained from Cox regression. Analyses adjusted for age, limitations in mobility and in activities of daily living, cognitive function, comorbidity (Charlson index), polipharmacy, renal function, NYHA functional class, treatment with β-blockers, and heart rhythm (atrial fibrillation or flutter vs sinus rhythm).

Results: A total of 256 patients (mean age 85.8 ± 5.8 years) were studied. Of them, 67% were women, and 58.5% received treatment with ACEI o ARB on discharge. Those treated with ACEI-ARB were younger (P = 0.006), had lower levels of creatinine (P = 0.001) and higher systolic arterial pressure at discharge (P = 0.003). ACEI-ARB treatment was used more frequently in those with diabetes (P = 0.001) and history of hypertension (P = 0.004), and less often in those with chronic renal failure (P = 0.04) and anaemia (P = 0.03). The accumulated 2-year mortality was 38% (33% in those with ACEI-ARB and 44.7% in those who didn't). In multivariate analysis, treatment with ACEI or ARB was associated with a lower mortality over 2 years (hazard ratio 0.62; 95% CI 0.40–0.94, P = 0.024).

Conclusions: In very old patients with HF and PVEF, treatment with ACEI or ARB is associated with improved survival. These results should be confirmed in randomized clinical trials.

Keywords: Heart failure; Elderly; Preserved systolic function; ACEI-ARB

PO-214

LEFT VENTRICULAR HYPERTROPHY IN OVERWEIGHT/OBESE HYPERTENSIVES WITH METABOLIC SYNDROME DEPENDS ON BODY MASS INDEX

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Overweight (ow) and obesity (ob) relate to blood pressure (BP) and left ventricular hypertrophy (LVH). It is unclear whether the presence of metabolic syndrome (MetS) independently affects echocardiographic parameters. The main aim of this study was to evaluate whether MetS is an independent risk factor for LVH in ow/ob, non-elderly, hypertensive patients. We expecially aimed to verify whether the relationship between MetS and LVH is independent from BMI.

Three hundred and eighty non elderly ow/ob patients under chronic stable treatment for essential hypertension were studied. MetS was defined according to NCEP III/ATP with AHA modifications and LVH as $LVM/h^{2.7} \geq 49.2\ g/m^{2.7}$ in males and $\geq 46.7\ g/m^{2.7}$ in females. Hypertensive patients with MetS had significantly higher BMI, systolic and mean BP, interventricular septum and relative wall thickness, and lower ejection fraction than those without MetS. $LVM/h^{2.7}$ was significantly higher in MetS patients (59.14 ± 14.97 vs $55.33 \pm 14.69\ g/m^{2.7}$; P = 0.022). Hypertensive patients with MetS had a 2.3-fold higher risk to have $LVH/h^{2.7}$ after adjustment for age, SBP, and therapy (OR 2.28; 95% CI 1.43–3.62; P = 0.001), but MetS lost its independent relationship with LVH when BMI was included in the model. Moreover, patients with MetS had a 2.8-fold higher relative risk to have CR (OR 2.81 95% CI 1.41–5.62; P = 0.002). In the subgroup of patients (n = 184, 48%) in which 24-hour ambulatory blood pressure measurements were available, the use of 24-hour SBP instead of office SBP confirmed the results, and the overall fit of the models actually improved.

Therefore, in ow/ob hypertensive patients MetS maintains its role of risk factor for LVH independently of age, SBP, and therapy, resulting in a useful predictor of target organ damage in clinical practice. However, MetS loses its independent relationship when BMI is taken into account, suggesting that the effects on MetS on LV parameters are mainly driven by the degree of adiposity.

Keywords: Left ventricular hypertrophy; Metabolic syndrome; Obesity; Hypertension

PO-215

THE ASSOCIATION OF LEFT VENTRICULAR HYPERTROPHY WITH EXERCISE INDUCED INTRAVENTRICULAR ASYNCHRONY

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Background: Left ventricular hypertrophy (LVH) is related to LV asynchrony at rest. Impaired exercise tolerance with dyspnea in hypertensive patients may be due to the exaggeration of nonuniform ventricular activation. The aim of study is to evaluate the effect of LVH on systolic intraventricular asynchrony during exercise.

Method: A total of 100 patients with hypertension complained of exertional dyspnea were enrolled. (mean age: 55.2 ± 11.3 years) Thirty-five patients were classified as having LVH. Exercise stress echocardiography was performed using a symptom limited, multistage supine bicycle. To evaluate the asynchrony of LV, we calculated standard deviation (SD) of averaged time-to-peak systolic velocity (TPV-SD, ms) of 12 middle and basal LV segments obtained from the three standard apical views at rest and peak exercise.

Results: There was no significant difference in gender, exercise duration, BP and HR between two groups. E/E' (index of diastolic filling pressure) was higher and systolic contractile reserve was decreased in LVH group. A value of TPV-SD was higher in patients with LVH at rest (31.5 ± 12.1 vs 22.0 ± 12.6 ms, P = 0.002) and this continued at peak exercise. (38.9 ± 11.9 vs 24.6 ± 13.3 ms, $P < 0.001$) Multiple regression analysis showed both enlarged LV chamber (β = 0.376, P = 0.009) and higher value of regional wall thickness (β = 0.393, P = 0.007) were independently associated with LV asynchrony at peak exercise.

Conclusion: The impairment of intrarventricular systolic synchronicity is related to LVH in patients with hypertension. This may be able to suggest the mechanism of the dyspnea on exertion in patients with hypertension.

Keywords: Intraventricular asynchrony; Left ventricular hypertrophy

PO-216

GENDER SPECIFIC PROGNOSTIC DIFFERENCES IN REGARD TO THE REGRESSION OF HYPERTENSIVE LEFT VENTRICULAR HYPERTROPHY (12 YEARS FOLLOW-UP STUDY)

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Aim: The aim of the present follow-up study was to evaluate gender-related prognostic differences in patients with hypertensive left ventricular (LV) hypertrophy in regard to the regression of LV mass.

Methods: A total of 73 age matched, nondiabetic, hypertensive male (n = 44, aged 55.4 ± 8 years) and female (n = 29, aged 57.3 ± 6 years) patients with echocardiographically proved LV hypertrophy, were analyzed for cardiovascular death, fatal or non-fatal myocardial infarction, fatal or non fatal stroke and revascularisation procedures after 12 year follow-up.

Results: No significant sex-differences were recorded at baseline for systolic (167.8 vs 161.3 mm Hg) and diastolic blood pressure (101.3 vs 97.7 mm Hg), LV mass (307.3 vs 300.6 g) and LV mass index (158.2 vs 162.6 g/m^2). After 12 years of follow-up LV mass significantly ($P < 0.05$) decreased in women and increased in men (-34 g vs +65 g), while blood pressure significantly ($P < 0.05$) decreased both in men (from 168/101 to 153/89 mm Hg) and women (from 161/100 to 159/94 mm Hg). Although body mass index, glucose and total cholesterol increased, while triglycerides decreased in both sexes, the number of male patients with metabolic syndrome increased (from 19 to 25), while it decreased in female (from 17 to 12). After 12 years of follow-up, fatal cardiovascular events were observed in five men (two sudden deaths, one stroke and one cardiovascular death), while one woman died after a fatal stroke. The composite endpoint, which included cardiovascular death, fatal or non-fatal myocardial infarction, fatal or non fatal stroke and revascularisation procedures, was significantly ($P < 0.05$) higher in men (31.8% vs 10%) at the end of the study period.

Conclusion: Significantly decreased LV mass and the prevalence of the metabolic syndrome in women with hypertensive LV hypertrophy were observed to be associated with lower rates of cardiovascular mortality and morbidity after 12 years of follow-up.

Keywords: Hypertension; Left ventricular hypertrophy; Metabolic syndrome

Hypertension in Patients With Chronic Kidney Disease

PO-217

PREDICTORS OF ADEQUATE CONTROL OF HYPERTENSION AMONG CHRONIC KIDNEY DISEASE PATIENTS (PREACH-CKD)

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There is no previous study describing the adequacy of hypertension treatment in adults with chronic kidney disease (CKD) in the Philippines, and analyzing the predictors of adequate control of blood pressure. We assessed adherence to known hypertension guideline targets for patients with CKD (blood pressure <130/80 mm Hg). We also evaluated determinants of adequate blood pressure control. Presence of CKD was defined as glomerular filtration rate <60 mL/min/1.73 m^2 or presence of albuminuria (urine albumin >30 g/dL). Multivariable logistic regression with appropriate weights was used to determine predictors of inadequate hypertension control. Among 72 participants with CKD, mean systolic blood pressure was 132.5 ± 18.6 mm Hg, and blood pressure was above target in 33% of patients. High BMI (t = 2.18, P = 0.048) and high total cholesterol (t = -2.1, P = 0.05) was found to be significantly associated with poor BP control.

We conclude that control of hypertension is poor in the studied subset of patients with CKD and that lack of control is primarily attributable to high BMI and high total cholesterol.

Table I. Predictors of systolic blood pressure control in patients with chronic kidney disease

Parameter (mean)	t	P
Age (years)	0.81	0.44
Female gender	−0.32	0.75
Educational attainment	-1.5	0.16
BMI	2.58	0.03
DM	1.7	0.11
CAD	0.58	0.61
Creatinine	1.9	0.09
GFR	0.76	0.47
CKD Stage	0.11	0.91
Uric acid	0.50	0.63
Albuminuria	-1.5	0.15
Total cholesterol	-2.1	0.05
LVH	1.3	0.24

BMI, Body mass index; DM, Diabetes; CAD, Coronary artery disease; GFR, Glomerular filtration rate; CKD, Chronic kidney disease.

Keywords: Hypertension; Chronic kidney disease; Dyslipidemia

PO-218

PREVALENCE, AWARENESS, TREATMENT AND CONTROL OF HYPERTENSION IN CHRONIC KIDNEY DISEASE

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The present study was designed to determine the prevalence, awareness, treatment and control rates of hypertension in chronic kidney disease (CKD) patients. The blood pressure (BP) data of the population (n: 10748) based national survey of CKD in Turkey (CREDIT study) was evaluated. CKD was defined as decrease of GFR below 60 mL/min/1.73 m^2 or presence of microalbuminuri, proteineuria. Hypertension was assumed to be present if there was a recorded diagnosis of hypertension or measured systolic BP was ≥140 mm Hg and/or diastolic BP was

≥90 mm Hg. The prevalence, aweraness, treatment and control rates of the hypertension in CREDIT population were 32.7%, 47%, 29.3% and 16.3%, respectively. In CKD group (15.7%) the prevalence of hypertension was 56.3% The prevalence at stage 1 CKD was 34.8% and increase to 79.8% at stage 3, reaching to 92.3% at stage 5 CKD. Only the 13.4% of patients with CKD have optimal BP. 60.9% of CKD patients were aware of hypertension and 41.7% were under pharmacological treatment. Overall control rate of hypertension (BP <140/90 mm Hg) in CKD group was 16.2% with the lowest rate at stage 1 (12.8%) and the highest at stage 4 (36.8%). The percent of the patients having BP <130/85 mm Hg in treated group was only 9.9%. In conclusion, despite the high prevalance, the awareness, treatment and control rates are low in CKD patients. Only 10% of CKD patients treated for the hypertension, have BP mesurements below the target level.

Keywords: Chronic kidney disease; Hypertension; Prevalence; Blood pressure control

PO-219

SELECTIVE ENDOTHELIN-A RECEPTOR ANTAGONISM REDUCES PROTEINURIA, BLOOD PRESSURE AND ARTERIAL STIFFNESS IN CHRONIC PROTEINURIC KIDNEY DISEASE

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Background: Proteinuria is associated with adverse cardiovascular and renal outcomes that are not prevented by current treatments. Endothelin-1 (ET-1) promotes the development and progression of chronic kidney disease (CKD), and associated cardiovascular disease (CVD). We therefore studied the effects of selective endothelin-A receptor antagonism with sitaxsentan in proteinuric CKD patients, assessing proteinuria, blood pressure (BP) and arterial stiffness (AS) – key independent, surrogate markers of CKD progression and CVD risk.

Methods: In a randomized double-blind, three-way crossover study, 27 subjects receiving recommended renoprotective treatment, received 6 weeks of placebo, sitaxsentan 100 mg od and nifedipine LA 30 mg od. Twenty-four hour proteinuria, protein:-creatinine ratio (PCR), 24 hour ambulatory BP, and pulse wave velocity (PWV; as a measure of arterial stiffness), were measured at baseline and week 6 of each treatment period. In 13 subjects, renal blood flow and glomerular filtration rate were assessed at baseline and week 6 of each period.

Results: Compared to placebo, sitaxsentan significantly reduced proteinuria (24 hour proteinuria by -0.62 ± 0.11 g/day, $P < 0.01$; PCR by -43 ± 8 mg/mmol, $P = 0.01$), BP (24 hour mean arterial BP by -4 ± 6 mm Hg, $P < 0.01$), and PWV by $-5 \pm 9\%$ ($P < 0.01$). Nifedipine matched the BP and PWV reductions seen with sitaxsentan. However, whereas sitaxsentan reduced proteinuria, nifedipine did not. Sitaxsentan alone reduced both glomerular filtration rate and filtration fraction. It caused no clinically significant side effects.

Conclusions: Sitaxsentan may provide additional cardiovascular and renal protection by reducing proteinuria, BP and arterial stiffness in CKD subjects already receiving optimal recommended treatment. The antiproteinuric effects of sitaxsentan likely relate to changes in BP and renal hemodynamics.

Keywords: Endothelin; Proteinuria; Hypertension; Chronic kidney disease

PO-220

DISCORDANT ESTIMATION OF THE PREVALENCE OF MASKED HYPERTENSION ACCORDING TO DAYTIME OR NIGHTTIME BLOOD PRESSURE IN SUBJECTS WITH CHRONIC KIDNEY DISEASE. THE HYGIA PROJECT

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Sleep-time blood pressure (BP) determined by ambulatory monitoring (ABPM) is a stronger predictor of cardiovascular (CVD) risk than awake or 24 hour BP means. However, isolated-office and masked hypertension (HTN) are commonly defined by comparing clinic with awake BP, disregarding the value of sleep-time BP, frequently elevated in subjects with chronic kidney disease (CKD). We evaluated the impact of sleep-time BP in the real prevalence of isolated-office and masked HTN in subjects with CKD participating in the Hygia Project, designed to evaluate cardiovascular risk by ABPM in primary care centers of Northwest Spain. We studied 1650 subjects with CKD (glomerular filtration rate <60 and/or microalbuminuria), 940 men/710 women, 67.4 ± 12.6 years of age. Among these, 1554 had HTN, defined as an awake BP mean ≥135/85 mm Hg for systolic/diastolic BP, or an asleep BP mean ≥120/70 mm Hg, or BP-lowering treatment. BP was measured by ABPM for 48 hour. Among uncontrolled hypertensive patients with CKD, 92.5% had nocturnal HTN. Using both awake as well as sleep-time BP thresholds in comparison with clinic BP (140/90 mm Hg), the prevalence of normal BP, isolated-office HTN, masked HTN and sustained HTN were 17.3%, 16.1%, 16.9% and 49.7%, respectively. Using only awake BP in comparison with clinic BP, the prevalence of the four classes were 25.8%, 26.7%, 8.4% and 39.1%, respectively ($P < 0.001$ compared to the previous classification). However, the prevalence obtained using only asleep BP for classification was 18.2%, 20.2%, 16.0% and 45.6%, respectively, very close to the classification obtained by using both awake and asleep BP means. Elevated sleep-time BP mean is a major factor for the proper diagnosis of HTN in patients with CKD. The common use of only awake BP mean in comparison with clinic BP values does not allow proper identification of over 50% of subjects with true masked HTN and thus high CVD risk. Both awake and asleep BP derived from ABPM must be used to diagnose HTN and to properly stratify CVD risk, especially in subjects with CKD.

Keywords: Chronic kidney disease; Masked hypertension; Sleep-time blood pressure

PO-221

ALTERATION OF THE CIRCADIAN BLOOD PRESSURE PATTERN IN SUBJECTS WITH CHRONIC KIDNEY DISEASE: THE HYGIA PROJECT

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Non-dipping in blood pressure (BP), elevated urinary albumin excretion and decreased glomerular filtration rate have all been associated with an increased cardiovascular risk. Some relatively small studies have suggested non-dipping is highly prevalent among subjects with chronic kidney disease (CKD). Accordingly, we studied the impact of CKD on the circadian BP pattern in subjects participating in the Hygia Project, designed to evaluate prospectively cardiovascular risk by ambulatory BP monitoring (ABPM) in primary care centers of Northwest Spain. We studied 6117 subjects (3326 men/2791 women), 61.7 ± 13.5 years of age. Among them, 1650 had CKD (glomerular filtration rate <60 and/or microalbuminuria; 1554 hypertensives). Hypertension was defined as an awake mean ≥135/85 mm Hg for systolic/diastolic BP, or an asleep mean ≥120/70 mm Hg, or BP-lowering treatment. BP was measured at 20-min intervals from 07:00 to 23:00 hour and at 30-min intervals at night for 48 hour. Among subjects without CKD, the prevalence of extreme-dipper, dipper, non-dipper and riser BP patterns were 4.7%, 47.2%, 42.3% and 5.9%, respectively. The prevalence of non-dipping and rising were significantly higher among subjects with CKD (49.8% and 16.5%, respectively; $P < 0.001$). Elevated nighttime BP above the thresholds provided above was the main cause for diagnosis of hypertension in CKD; thus, 92.5% of the uncontrolled hypertensive subjects with CKD had nocturnal hypertension, while only 71.3% had diurnal hypertension. This cross-sectional study documents the high prevalence of an altered circadian BP pattern in CKD. The prevalence of rising, associated with the highest cardiovascular risk of all BP patterns, is almost three times higher among subjects with CKD. The elevated nighttime BP mean in CKD leads to a very high prevalence of nocturnal hypertension and, thus, to misdiagnosis of hypertension when relying only on clinic or even awake BP mean values. These findings support ABPM as a requirement for proper diagnosis and cardiovascular risk assessment in subjects with CKD.

Keywords: Chronic kidney disease; Sleep-time blood pressure; Ambulatory blood pressure

PO-222

USEFULNESS OF THE RESISTIVE INDEX IN RENAL DOPPLER ULTRASONOGRAPHY AS AN INDICATOR OF VASCULAR DAMAGE IN PATIENTS WITH RISKS OF ATHEROSCLEROSIS

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In the present study, we investigated whether Resistive Index (RI) in renal Doppler ultrasonography (RDU) could be used to evaluate the pathogenesis of renal damage and predict the renal prognosis, and investigated the correlation between RI and blood pressure fluctuations or carotid thickening/carotid plaque in patients with or without hypertension.

Study subjects were a total of 194 patients (mean age: 66.2 years), who underwent RDU in our hospital ward between February 2009 and July 2010. We investigated the correlation between RI and multiple clinical parameters, including ambulatory blood pressure monitoring (ABPM) and carotid doppler examination.

RI was significantly correlated with the age, eGFR, diastolic blood pressure (BP), pulse pressure, and level of serum albumin and plaque score evaluated with carotid doppler examination. Patients with diabetes mellitus (DM) showed a significantly higher RI than patients without DM, although their eGFR was similar; thus, DM might accelerate renal vascular damage and RI could detect earlier changes of vascular damage proceeding the time eGFR is reduced. Regarding ABPM, patients with a larger morning surge (systolic BP in the early morning – lowest systolic BP during sleep) showed a significantly higher RI.

In conclusion, the present study indicated that RI might be very useful for the evaluation of very early renal damage more effectively than eGFR, and that diurnal BP change might be a risk factor for the progression of atherosclerotic change in the kidney evaluated by RI, so diurnal BP change should be considered as a therapeutic target for renal protection. Thus, RI evaluated by RDU may be very useful for the management of patients with CKD.

Keywords: Chronic kidney disease; Hypertension; Renal doppler ultrasonography; Resistive index

PO-223

INTRADIALYTIC HYPERTENSION IS NOT ASSOCIATED WITH INCREASED BLOOD PRESSURE VARIABILITY

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Hemodialysis (HD) patients have a high BP burden and increased BP variability (BPV). In hypertensive non-HD chronic kidney disease patients, increased BPV correlates with higher BP and adverse cardiovascular outcomes. Intradialytic HTN, defined as increases in systolic BP from pre to post-HD, occurs in up to 15% of HD patients and is also associated with increased morbidity and mortality. We sought to determine whether patients with intradialytic HTN have greater BPV during the interdialytic period than those without intradialytic HTN.

Between June 2009 and September 2010, we enrolled 50 maintenance HD patients into a case-control cohort study. Inclusion criteria was age 18–80 years, HD vintage >1 month, and HTN defined as pre-HD SBP ≥140 mm Hg or post-HD SBP ≥130 mm Hg. Cases were defined as subjects with intradialytic HTN (average pre to post-HD SBP increases ≥10 mm Hg in four out of six HD sessions) and controls were defined as subjects with pre to post-HD SBP decreases ≥10 mm Hg in four out of six sessions. Following a midweek HD session, 44-hour interdialytic ambulatory BP measurements were obtained using Spacelabs 90207. The primary outcome was BPV, assessed by the mean of all individual standard deviations (SD) of 44-hour ambulatory BP, which was compared between groups with an unpaired *t*-test. Daytime and nightime BPV were also analyzed.

The mean age of the 50 subjects was 55 years; 80% were male, 60% Hispanic, 38% African American, and 86% were diabetic.

Ambulatory SBP was higher in the intradialytic HTN group with a trend towards higher ambulatory DBP. However, there was no difference in BPV between groups during the entire 44-hour, daytime, or the nighttime period for SBP or DBP (Table I).
Compared to controls, patients with intradialytic HTN do not exhibit higher BPV, despite having higher ambulatory SBP. Mechanisms other than higher BPV should be investigated to explain the higher adverse event rates previoulsy identified among patients with intradialytic HTN.

Table I.

Ambulatory BP (mm Hg), (SD)	Intradialytic HTN (n = 25)	Control (n = 25)	*P*-value
44-hour SBP	155 (±14.2)	142 (±16.5)	0.005
SD of 44-hour SBP	16.5 (±5.5)	17.2 (± 3.4)	0.57
SD of daytime SBP	15.8 (±5.1)	17.0 (±3.7)	0.33
SD of evening SBP	14.8 (±7.8)	15.6 (±4.0)	0.68
44-hour DBP	82.2 (±11.0)	76.9 (±8.6)	0.06
SD of 44-hour DBP	10.0 (±2.5)	10.2 (±2.5)	0.80
SD of daytime DBP	9.7 (±2.5)	10.1 (±2.6)	0.51
SD of evening DBP	8.7 (±3.6)	9.8 (±2.3)	0.20

Keywords: Intradialytic hypertension; Blood pressure variability; Ambulatory blood pressure; Hemodialysis

PO-224

EFFECT OF VITAMIN D SUPPLEMENTATION ON BLOOD PRESSURE AMONG HD PATIENTS UNDERGOING DIALYSIS

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Study goal was to determine if the blood pressures of hemodialysis patients are reduced when their vitamin D deficiencies are corrected.
This is a retrospective evaluation of HD patients with vitamin D deficiency who received vitamin D supplementation. Patients with low 25 OH vitamin D level in sera were given vitamin D supplements 1000 units daily to raise the 25OH vit D level. Data on pre and post dialysis weights, total UF during dialysis and systolic and diastolic BP were retrieved from computerized medical records. The average systolic and diastolic BP readings, weights and UF before and after correction of vitamin D deficiency were compared.
Twenty eight patients on HD with vitamin D deficiency were given supplementation. Vitamin D was given at a dose of 1000 units daily and it increased average serum level from 14.16 ± 6.78 to 30.07 ± 11.37. There was no significant difference between pre-dialysis weights before and after vitamin D supplementation ($P = 0.340$). But there was a decrease in the average post-dialysis weight after vitamin D supplementation (87.15 ± 18.41 to 84.76 ± 18.34, $P = 0.243$). Pre-dialysis systolic and diastolic blood pressures both increased significantly after vitamin D deficiency was corrected (143.92 ± 21.62 to 152.46 ± 23.80 and 78.98 ± 14.95 to 83.78 ± 17.12, $P = 0.008$ and $P = 0.007$ respectively). Post-dialysis systolic and diastolic blood pressures also increased significantly after vitamin D (136.48 ± 22.48 to 143.54 ± 24.26 and 74.29 ± 12.18 to 77.82 ± 16.10, $P = 0.029$ and $P = 0.014$ respectively).
Vitamin D supplementation has increased pre or post dialysis blood pressure in hemodialysis patients with Vitamin D deficiency.

Keywords: Vitamin D deficiency; Blood pressure; Kidney disease; Dialysis

PO-225

HEME OXYGENASE INDUCTION PREVENTS ENDOTHELIAL DYSFUNCTION AND RENAL DAMAGE IN EC-SOD KO MICE

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Extracellular superoxide dismutase (ec-SOD, SOD3) regulates cellular redox status via dismutation of superoxide anion (O_2^-) to H_2O_2. Although, there is evidence linking SOD3 deficiency to essential hypertension and endothelial dysfunction a mechanistic evaluation of such causality needs further examination. We examined the effect of ec-SOD gene deletion on renal morphology, vascular function and reno-vascular heme oxygenase (HO)-adiponectin system. Experimental results were contrasted in wild type, ec-SOD-/- and ec-SOD-/- mice undergoing HO induction via cobalt protoporhyrin (CoPP). On histological examination ec-SOD-/- mice showed marked cortical, medullary and microvascular damage as compared to WT mice and although, ec-SOD-/- animals have increased HO expression, HO activity is significantly ($P < 0.05$) attenuated. These observations are accompanied with aortic endothelial dysfunction, reduction in levels of serum adiponectin and vascular epoxides (EETs). In addition, ec-SOD deficient animals demonstrate increase in apoptosis signal-regulating kinase-1 (ASK-1) ($P < 0.01$) along with reduced basal levels of p-eNOS, Bcl-XL and p-AKT. HO induction successfully rescues histopathological abnormalities in conjunction with restoration of vascular function, HO activity, EET production and serum adiponectin levels in ec-SOD-/- mice. Protein expression of molecular markers such as p-eNOS, p-AKT and Bcl-XL are also normalized in animals exposed to CoPP. In conclusion, increased oxidative stress in ec-SOD KO animals perturbs reno-vascular HO-adiponectin-EET pathways resulting in endothelial dysfunction along with renal damage. These findings support the hypothesis that the basal level of ec-SOD participate in maintaining vascular integrity and cellular defense mechanisms against oxidative stress by modulating HO system, epoxides, e-NOS, p-AKT, and adiponectin.

Keywords: Heme oxygenase; Extracellular superoxide dismutase; Oxidative stress; Adiponectin

PO-226

MEAN HEMODIALYSIS-UNIT SYSTOLIC BP IS SIMILAR IN PATIENTS WITH AND WITHOUT FREQUENT INTRADIALYTIC HYPERTENSION

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Intradialytic hypertension, defined as increases in systolic BP (SBP) from pre to post-hemodialysis (HD), is associated with increased mortality in the HD population. Compared to HD controls, HD patients with recurrent intradialytic HTN have been shown to have lower pre-HD SBP, higher post-HD SBP, and higher overall *inter*dialytic ambulatory SBP. We hypothesized that mean SBP obtained from the HD unit over 6 months would be higher among patients who experience intradialytic HTN more frequently.
We analyzed pre and post-HD SBP measurements among prevalent HD patients in our HD units from February to August 2010. Intradialytic HTN was defined as an increase in

SBP ≥ 10 mm Hg from pre to post-HD, and subjects were separated into quartiles based on the percentage of sessions where intradialytic HTN occurred. The primary endpoint was mean HD-unit SBP, which was calculated from the mean of all pre and post-HD SBP, and compared between quartiles using Analysis of Variance and the Tukey test. Mean pre-HD and mean post-HD SBP were also compared between quartiles.

Of the 362 subjects the mean age was 54.3 years; 60% were male, 59% African American, 34% Hispanic, and they had a mean of 63 HD sessions. The 25th, 50th, and 75th percentiles for percentage of HD sessions with intradialytic HTN were 8.93%, 17.83%, and 31.43%. The mean HD-unit SBP for the 1st through 4th quartiles were 143.9, 144.8, 145.6, and 145.6 mm Hg, respectively ($P = 0.76$) (Figure 1). (Figure 1) There were significant differences between quartiles regarding mean pre-HD SBP (158.2, 152, 149.1, and 142.3 mm Hg; $P < 0.0001$) and mean post-HD SBP (129.7, 137.7, 142.1, and 148.9 mm Hg; $P < 0.0001$) (Figure 1).

Increased frequency of intradialytic HTN is not associated with higher mean HD-unit SBP. SBP patterns during HD may be more prognostic of outcomes than pre-HD, post-HD, or averaged SBP measurements. What remains unknown among patients with similar mean HD unit SBP is whether the patients with more frequent episodes of intradialytic HTN have higher *inter*dialytic SBP burden.

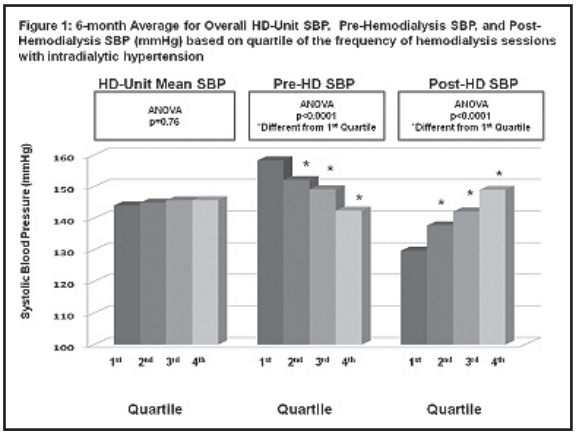

Figure 1: 6-month Average for Overall HD-Unit SBP, Pre-Hemodialysis SBP, and Post-Hemodialysis SBP (mmHg) based on quartile of the frequency of hemodialysis sessions with intradialytic hypertension

Keywords: Hypertension; Hemodialysis; End-stage renal disease

Kidney and Hypertension

PO-227

NIGHTTIME HEMODYNAMICS AND ARTERIAL STIFFNESS EXERT A POWERFUL ADDITIVE PREDICTIVE EFFECT ON THE OCCURRENCE OF MICROALBUMINURIA IN HYPERTENSION: A 6-YEAR FOLLOW-UP STUDY

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Nighttime blood pressure and arterial stiffness are related to target organ damage and increased cardiovascular risk. In this study we sought to investigate whether aortic stiffening defined by carotid-femoral pulse wave velocity (PWV) has either additive or synergistic effect with ambulatory BP load in the development of microalbuminuria during follow-up.

One hundred and sixty-three white hypertensive non-diabetic patients (52 ± 10 years, 98 men, 59 smokers, body mass index = 28.8 ± 5.4 kg/m^2) were prospectively studied for 6 years. All patients underwent 24-hour ambulatory monitoring and PWV measurement with Complior SP. Metabolic profile, estimated creatinine clearance (eGFR) and echocardiographic measurements were performed at baseline and last outpatient clinic visit (follow-up: 4.5 ± 0.89 years). Microalbuminuria was defined as ACR between either 20 or 30 (men and women respectively) and 300 mg. All subjects were under optimal antihypertensive therapy complemented by vasoactive drugs where appropriate. The administered medication during the last 6-month period before last visit consisted of: renin-angiotensin system inhibitors RAASI (49%), diuretics (25%), calcium-channel blockers (20%), β-blockers (13%), statins (16%) and antiplatelet agents (18%).

Baseline nighttime systolic and diastolic BP were 121 ± 13 and 73 ± 9 mm Hg, while the incidence of microalbuminuria was 13.5% (n = 22). Between baseline and last visit there was a decrease in BMI by 1.9 ± 4.1 Kgr/m^2, while PWV was increased by 1.83 ± 1.37 m/s (7.9 ± 1.5 vs 9.6 ± 1.5 m/s). During follow-up, 24 hour systolic and diastolic BP were decreased by 12.7 ± 9.1 and 8.2 ± 6.2 mm Hg (130 ± 12 vs122 ± 12 and 80 ± 9 vs 75 ± 8 mm Hg) respectively. In Cox regression models after adjustment for confounders, independent predictors (HR [95% CI]) of microalbuminuria were: baseline nighttime systolic BP, 1.034 [1.001–1.068], $P = 0.046$, baseline PWV, 1.317 [1.048–1.654], $P = 0.018$, and the interaction term of nighttime systolic BP × baseline PWV, 1.003 [1.001–1.004], $P < 0.001$.

Baseline nocturnal systolic BP and PWV have an additive effect on the development of microalbuminuria suggesting that integrated stiffening measures may predict renal damage in the early stages of hypertension.

Keywords: Nocturnal blood pressure; Arterial stiffness; Microalbuminuria; Hypertension

PO-228

LEARNING NEPHROLOGY THROUGH MOBILE DEVICES: THE NEPHROLOGY ON-DEMAND MOBILE EXPERIENCE

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Increasingly, healthcare providers (HCP) consume medical information through mobile devices, but the popularity of these devices is unknown. Medical educators who provide information online need to know how learners may utilize mobile devices to obtain information if they wish to communicate effectively. This knowledge will guide IT resource allocation and medical website development. We characterized how HCPs use mobile devices to access a medical education website.

Nephrology-related medical information was made available to all mobile devices through Nephrology On-Demand (NOD) Mobile, a website maintained by the Division of Nephrology at East Carolina University. It contains evidence-based Nephrology teaching material categorized by topic, date, and target audience. Computer code from WPTouch was included in the website's root files to display a mobile-specific version of the website when accessed through a mobile device. Google Analytics code was included to track visits, pageviews, time on site, bounce rate, location, connection speed, device type, and browser type for all mobile devices. New and return visits were calculated using IP addresses and cookies. Data was collected from 02/10 to 10/10.

Six hundred and thirty-eight mobile visits were made during the study period (5.4% of total visits) from four areas of the world (USA 91%, Europe 3%, and Asia 4%, Central and South America 2%). Four hundred and forty-one visits (71%) were from Apple iPhones. Adobe Flash-compatible devices comprised 16% of visits. Fifty-five percent of all visits were through a cellular connection As a result of the slower connection speed, these users spent the most time on the website (264 s/visit). Users connected via faster speeds spent less time but viewed more resources than those using a cellular connection (97–158 s/visit for 2.14–2.65 resources/visit).

Data from NOD Mobile can guide educators in developing user-friendly teaching tools in an attractive platform. Educators should prioritize Apple iPhone users when allocating IT resources. Adobe Flash-compatible teaching resources should be avoided if one wishes to address the largest audience. Educators contemplating using mobile devices should initially develop English-only resources. Teaching resources should be programmed to load quickly through cellular connections, as they are the most commonly used. Further investigation on education using mobile devices is underway.

Keywords: Education; Internet; Online; Teaching

PO-229

CHARACTERISTICS OF HYPERTENSIVE PATIENTS USING EITHER ALISKIREN OR OTHER ANTIHYPERTENSIVE MEDICATIONS

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Objective: The purpose of this study was to compare demographic and clinical characteristics among hypertension patients treated with aliskiren or other antihypertensive agents (AHYs) in a large, commercially insured population.

Methods: This observational cohort study queried the HealthCore Integrated Research Database (HIRD^{SM}) of approximately 38 million commercially insured members to identify patients ≥18 years old, with ≥1 medical claim with ICD-9 code(s) 401.xx-404.xx for hypertension on or before the index date, defined as the date of the first pharmacy claim for aliskiren or another AHY between January 1, 2007 through November 30, 2008. Patients were required to have ≥12 months of continuous eligibility prior to their index date, but were not required to be AHY treatment naïve prior to index therapy. Demographic and clinical characteristics during the 12 month pre-index period were compared.

Results: Aliskiren patients (n = 8062) were of similar age as patients taking other AHY agents [n = 845,874; mean age (±SD) 60.4 (±12.9) vs 57.8 (±13.6), respectively] and had a similar gender distribution (53% and 51% were male, respectively). Sixteen percent of aliskiren prescribers were nephrologists or cardiologists, as compared to 8.1% of other AHY users. Aliskiren patients were more likely to use β blockers (38% vs 31%), diuretics (15% vs 5%) and CCBs (28% vs 19%) but less likely to use ACEIs (16% vs 31%) during the 30 days ± index date compared to other AHY users. Aliskiren patients had more AHY use prior to their index drug [15.8 (±13.1) vs 9.0 (±10.3)] and a higher Deyo-Charlson Comorbidity index [1.4 (±1.9) vs 0.9 (±1.5)], with increased rates of comorbidities, including diabetes (36% vs 21%) and CKD (14% vs 4%). Multivariate regression indicated that patients with the following characteristics were more likely to be prescribed with aliskiren: diabetes ($P = 0.015$), CKD ($P = 0.0001$), greater pill burden ($P < 0.0001$), higher total healthcare costs ($P < 0.0001$) and a longer duration of HTN during the pre-index period ($P < 0.0001$).

Conclusion: Overall, aliskiren patients used more AHY medications, had more comorbidities and longer duration of HTN in the pre-index period compared to other AHY users. This disease severity reflected in the higher proportion of specialists prescribing aliskiren.

Keywords: Aliskiren; Hypertension; Comorbidities

PO-230

THE DOPAMINE D1-LIKE RECEPTORS INTERACT WITH THE A_{1A} ADRENERGIC RECEPTOR IN HUMAN RENAL EPITHELIAL TUBULE CELLS

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As a multifactorial disorder, essential hypertension is influenced not just by the individual's lifestyle and environment but also by the interplay of a myriad of physiologic systems that either promote or protect against sustained increase in blood pressure. The D1-like dopamine receptors (D_1R and D_5R) and the α_{1A} adrenergic receptor ($AR\alpha_{1A}$) are endogenously expressed in the kidney and promote contrasting effects on sodium transport, resulting in either natriuresis (D_1R and D_5R) or anti-natriuresis ($AR\alpha_{1A}$). We tested the hypothesis that the D_1R and D_5R interact with $AR\alpha_{1A}$ in human renal proximal tubule cells (hPTCs). We found that D_1R and D_5R co-immunoprecipitated endogenous $AR\alpha_{1A}$ and pulled-down heterologous $AR\alpha_{1A}$-myc,His in hPTCs, where treatment with the D1-like receptor agonist fenoldopam (1 μmol/L per 15 minutes) enhanced the interaction. D_1R and D_5R also colocalized with $AR\alpha_{1A}$ in HEK293 cells, in which fenoldopam increased their colocalization at the perinuclear area, and in proximal tubules (and distal tubules for D_5R) in human kidney sections. Prolonged (24-hour) fenoldopam treatment resulted in decreased D_1R (70.0 ± 5.9% vs 100 ± 3.7%, $P < 0.05$, n = 3) and D_5R (50.1 ± 10.7% vs 100 ± 10.7%, $P < 0.05$, n = 3) and increased $AR\alpha_{1A}$ abundance (142.6 ± 4.3% vs 100 ± 6.4%, $P < 0.05$, n = 3) in hPTCs, suggesting that the D1-like dopamine receptors may regulate the expression of $AR\alpha_{1A}$. Understanding the interaction between these receptors is essential to comprehending the crosstalk between anti- and pro-hypertensive systems.

Keywords: Dopamine receptor; Alpha1A adrenergic receptor; Kidney; Proximal tubule cell

PO-231

UNCOUPLED NOS IS A MAJOR SOURCE OF RENAL SUPEROXIDE IN ANGIOTENSIN II-INDUCED HYPERTENSION

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Angiotensin II increases superoxide production in the kidney and this has been implicated in sodium retention and vasoconstriction leading to hypertension. The NADPH oxidases have been implicated as a source of superoxide in the setting of hypertension and high salt diet. Another potential superoxide source is uncoupled nitric oxide synthase (NOS). NOS-uncoupling can occur when levels of tetrahydrobiopterin (BH_4) are insufficient. We hypothesized than angiotensin II would cause NOS-uncoupling and sought to determine mechanisms underlying this phenomenon.

To test this we treated C57Bl/6 mice with angiotensin II (490 ng/kg/min) for 2-weeks and measured superoxide using dihydroethidium and HPLC and pterin levels using HPLC in the renal medulla and cortex. We found that angiotensin II infusion for 2 weeks increases renal medullary $O_2^{\cdot-}$ production (from 29 ± 3 to 48 ± 3 pmol/mg, $P < 0.005$) and to a lesser extent in the cortex (from 35 ± 4 to 52 ± 7 pmol/mg). Surprisingly, we found that NADPH oxidase activity was not augmented by angiotensin-II. In contrast, the NO synthase (NOS) antagonist L-NAME abolished the increase in $O_2^{\cdot-}$ in both cortex and medulla, indicating uncoupled NOS as the source of renal $O_2^{\cdot-}$ in hypertension. These data is supported by the evidence of angiotensin II inhibition of NOS dimer formation as measured by low-temperature SDS-PAGE inmmunoblot. In studies to determine why angiotensin II causes NOS uncoupling we found that angiotensin II-infusion dramatically decreased total pterins in both the medulla (11.8 ± 6 to 3.2 ± 0.5 pmol/mg, $P < 0.05$) and cortex (10.5 ± 3.4 to 3.6 ± 0.1 pmol/mg, $P < 0.05$) as well as the oxidized pterin BH_2. Further studies showed that the rate limiting enzyme for BH_4 production, GTP cyclohydrolase-1 (GTPCH-1), was unchanged by western blot and enzyme activity assay. Urine measurements showed that angiotensin-II induces renal loss of pterins. We conclude that hypertension is associated with a profound depletion of renal pterins, leading to NOS uncoupling, at least in part by increased urinary excretion.

Keywords: NOS, nitric oxide synthase; BH4, tetrahydrobiopterin

PO-232

LOSS OF SNX5 IMPAIRS DOPAMINE D_1 RECEPTOR ENDOCYTOSIS AND RECYCLING AND AGGRAVATES THE BLOOD PRESSURE IN SHR

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Endocytosis and recycling of cell surface dopamine receptors subsequent to ligand-dependent activation are mechanisms that allow cells to modulate their response to external stimuli. Although much has been learned about the internalization of these receptors, comparatively little is known about their trafficking and recycling. Here we report the discovery of a dynamic spatial and temporal relationship between sorting nexin 5 (SNX5) and the D_1 dopamine receptor (D_1R). Through confocal and FRET-FLIM microscopy, we show that the internalization of agonist-stimulated D_1R is mediated by SNX5 in human proximal tubule cells. About 50% of surface D_1R were internalized in control cells, while no receptor endocytosis was observed with SNX5 silencing ($P < 0.05$, n = 3). Transfection of inactivating anti-SNX5 antibody resulted in delay in the recycling of the receptor to the membrane. RNAi-mediated silencing of SNX5 results in the failure of D_1R to increase cAMP after agonist (fenoldopam, 1 μmol/L per 15 min) stimulation. Moreover, subcapsular infusion of Snx5-specific siRNA into the rat kidney results in decreased sodium excretion ($\Delta = -0.2 \pm 0.005$ mEq/mg creatinine, $P < 0.05$, n = 5/group) and increased blood pressure ($\Delta = 48 \pm 5$ mm Hg, $P < 0.05$, n = 5/group). Our results indicate that SNX5 is essential for the intracellular trafficking and function of the D_1 dopamine receptor and that renal-specific loss of SNX5 in the SHR decreases the natriuresis and further increases the elevated blood pressure in this genetic model of hypertension.

Keywords: Dopamine D1 receptor; Sorting nexin 5; Receptor endocytosis; Receptor trafficking

PO-233

AMBULATORY BLOOD PRESSURE MEASUREMENT IN PATIENTS WITH CHRONIC KIDNEY DISEASE: OUTCOMES AND CORRELATION WITH CLINIC BP AND BPTRU

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Objective: This is a pilot study to determine the pattern of hypertension and the 24 hour blood pressure control in patients of chronic kidney disease (CKD) using ambulatory BP monitoring (ABPM) and correlate the findings with clinic BP (CLBP) measurements and BpTRU.

Methods: Thirty consecutive hypertensive CKD (stage II–V) underwent CLBP measurement by Sphygmomanometer followed by Oscillometric method using the automated device called BpTRU. Thereafter 24 hour ABPM was done.

Results: Sixty percent (n = 18) of the study population had blood pressure overload. Of these 16 had systolic overload; 11 had systolic and diastolic overload and only two had isolated diastolic BP overload.
The average pulse pressure was high (48 mm Hg).
The prevalence of WCH was 33% (n = 10). In these patients BpTRU correlated better ($P = 0.2$) with 24 hour ABPM readings as compared to Clinic BP ($P = 0.05$).
Thirty percent (n = 9) patients had masked hypertension (normal Clinic BP but >50% readings above normal in 24 hour ABPM). The BpTRU readings were also significantly different from the ABPM readings

Conclusions: In CKD patients, single Clinic BP readings failed to detect White Coat Hypertension and Masked Hypertension, and are a poor indicators of overall blood pressure control. Since these parameters have important therapeutic and prognostic implications, we recommend periodic 24 hour ABPM as a clinical guide for adjustment of anti-hypertensive therapy to achieve BP targets in CKD. For the first time in Indian CKD patients we have shown that the BpTRU can be a very useful and cost effective alternative in assessment of White Coat Hypertension.

Keywords: BpTRU; Ambulatory blood pressure; Chronic kidney disease; White coat hypertension

PO-234

PERINATAL DIETARY PROTEIN AND NACL ON OFFSPRING'S AMBULATORY BLOOD PRESSURE AND RENAL INJURY

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Low protein-high salt diets may result in a high incidence of renal failure and increased blood pressure (BP). The role of maternal diets on progeny susceptibility and effects of perinatal dietary protein and NaCl were tested in renal injuries and BP in Lewis rats with 10% low protein (LP) and 23% normal protein (NP) and/or NaCl (4% high, HS; 0.6% normal, NS) diets starting at pre-pregnancy through pups' weaning at day-21. Pups were on

either a 4% NaCl (hs) or 0.6% NaCl (ns) diet and at 13–14 weeks of age, telemetry monitored BPs were collected every 10-min and analyzed by methods of linear least square rhythmometry and ANOVA. Offspring in LPHS had significantly increased BPs (in mm Hg): NPNSns, 133 ± 2 vs LPNSns, 138 ± 1 and LPNShs, 138 ± 1, both $P < 0.05$; NPNSns, 133 ± 2 vs LPHShs, 142 ± 2, $P < 0.01$). All LP groups exhibited significantly lower body weight (BW). Glomerular filtration rates (GFR, inulin, mL/min) were compared. After a high protein diet was given overnight, significantly smaller GFR changes were observed, especially in NPHShs and all LP- as compared to NPNS groups: NPNSns, 0.935 ± 0.28; NPNShs, 0.927 ± 0.2; NPHSns, 0.537 ± 0.17; NPHShs, −0.064 ± 0.13; LPNSns, −0.229 ± 0.06; LPNShs, 0.057 ± 0.16; LPHSns, −0.515 ± 0.17; LPHShs, −0.404 ± 0.27. Kidney weight/BW was compared: 0.0038 ± 0.0001; 0.0045 ± 0.0001; 0.0039 ± 0.0001; 0.0044 ± 0.0001; 0.0038 ± 0.0001; 0.0043 ± 0.0001; 0.0038 ± 0.0001; 0.0043 ± 0.0001, respectively (hs vs ns, all $P < 0.001$). Reduced sclerotic glomerular numbers (GN) were observed when low calorie (LC) diet was introduced in a subset of two groups with either normal or low calorie diet (15.68 ± 1.5 vs 11.19 ± 1.2, $P < 0.001$), though GN were similar in both groups (113 vs 111 per kidney cross section, P = NS). In comparisons of the three-way interaction, perinatal protein and salt, and offspring diets significantly affected offspring's BP ($P < 0.014$), while protein diet alone affected offspring's BP, GFR and BW significantly (P = 0.001, 0.0001, and 0.0001, respectively). Salt significantly affected BP (P = 0.005) and GFR changes (P = 0.0001). Effects of maternal proteins and offspring together were significant on BP (P = 0.047) and GFR changes (P = 0.013). Thus, the current study indicates that perinatal LP and HS diets significantly affect offspring's BP, renal injuries and kidney functions later in the offspring's life, especially when pups are on hs-diets.

Keywords: Perinatal diets; Ambulatory blood pressure; Glomerular filtration rate; Renal injury

PO-235

EFFECTS OF A DIRECT RENIN INHIBITOR ON RRI IN HYPERTENSIVE PATIENTS

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Background: Target organ damage is a powerful predictor of CV disease in hypertension. Renal Resistive Index (RRI) is a Pulse Doppler parameter which is considered an index of target organ damage at renovascular level. ACE-Inhibitors and Angiotensin Receptor Blockers (ARB) block Renin Angiotensin System (RAS), but upregulate plasma renin activity. In contrast the new antihypertensive drugs Aliskiren block the SRA and reduces plasma rennin activity.

Aim of the Study: to investigate in hypertensive patients with cardiac damage the effects on RRI of 1 year treatment with Angiotensin Receptor Blockers (ARB) alone in comparison to Aliskiren and ARB togheter.

Methods: A total of 100 patients, selected on presence of left ventricular hypertrophy at Echocardiography, were enrolled in an open-label 12 months parallel study. Excluding criteria were: diabetes mellitus, acute coronary syndrome and acute cerebrovascular syndrome. Patients were divided in two homogeneous groups. Data analysis included blood pression and RRI before treatment (baseline), after 3 and 12 months of treatment. RRI was assessed as: Systolic peak velocity – telediastolic velocity/systolic peak velocity

Results: Treatment reduced BP in both groups. reduction was greater after 12 months treatment in both groups. treatment with ARB plus Aliskiren. The treatment induced a biphasic response of rri in group treated with ARB alone: a slight decrease in month 3 followed by the tendency to return to baseline at 12 months. Vice versa, in group treated with ARB and Aliskiren RRI decresed at 3 months and stayed decreased at 12 months (Figure 1).

Conclusions: The blockade of the RAS by ARB togheter with inhibition of Renin activity by Aliskiren induces a greather antihypertensive effect and a more sustained reduction of RRI in comparison to blockade of SRA by ARB alone.

	ARB plus Aliskiren			ARB		
	baseline	3 months	12 months	baseline	3 months	12 months
N	50	50	50	50	50	50
Age (years)	52±10			53±10		
SBP (mmHg)	148±14	135±6	134±8	150±12	146±13	143±15
DBP (mmHg)	94±7	84±6	84±7	95±7	88±7	86±7
RRI	78±3	63±6	64±3	77±2	64±7	69±5

Keywords: Aliskiren; Renal resistive index

PO-236

UNCONTROLLED HYPERTENSION IN CKD PATIENTS IS ASSOCIATED WITH HIGHER HEART RATE

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A possible role of heart rate (HR), a surrogate of sympathetic nerve activity (SNA), in blood pressure control in patients with chronic kidney disease (CKD) and hypertension (HTN) was studied.

Seven thousand five hundred and eighty-nine reports of ABPM were analyzed. We excluded patients aged <18 and >80 years, atrial fibrillation, pregnancy and not receiving antihypertensive treatment. In patients with CKD [albuminuria >30 mg/day, GFR <60 mL/min] controlled HTN (c-CKD-HTN) was defined as: BP ≤135/75 during awake, and ≤120/70 at night (n = 165), uncontrolled (u-CKD-HTN) as: BP ≥140/90 during awake, ≥125/75 at night (n = 154). In addition, patients with essential HTN: controlled (c-HTN, n = 388) and uncontrolled (u-HTN, n = 300) were analyzed. Forty-three percent of CKD patients were diabetic. All results were adjusted for sex, age and BMI.

The average mean ± SEM of systolic BP (daytime, night-time) were: 119.2 ± 0.4, 105.7 ± 0.5 in c-CKD-HTN; 119.1 ± 0.3, 105.4 ± 0.3 in c-HTN; 159.4 ± 1.1, 148.6 ± 1.3 in u-CKD-HTN; 156.4 ± 0.6, 143.0 ± 0.7 in u-HTN, respectively, $P < 0.0001$. The average values of diastolic BP (daytime,

night-time) were: 68.5 ± 0.5, 58.6 ± 0.4 in c-CKD-HTN; 69.4 ± 0.3, 58.5 ± 0.3 in c-HTN; 95.1 ± 0.5, 86.2 ± 0.7 in u-CKD-HTN; 95.3 ± 0.3, 84.5 ± 0.4 in u-HTN, respectively, $P < 0.0001$. HR in uncontrolled HTN was higher compared with controlled HTN.

HR appears to be an important factor in BP control in patients with CKD and with essential HTN, whether or not BB are being used. We suggest that increased SNA may contribute to poorly controlled HTN in these patients.

Table I. Heart Rate in Patients with CKD and Essential Hypertension

Heart rate, beats per min.	c-CKD-HTN	u-CKD-HTN	c-HTN	u-HTN
Daytime				
β-blockers+	64.7 ± 0.9	75.2 ± 1.2*	66.6 ± 0.5	74.6 ± 1.1**
β-blockers-	71.6 ± 1.1	79.3 ± 1.2*	70.6 ± 0.7	75.8 ± 0.6**
Night-time				
β-blockers+	59.0 ± 0.8	66.9 ± 1.1*	59.2 ± 0.4	65.5 ± 0.9**
β-blockers-	61.2 ± 0.9	68.5 ± 1.1*	60.1 ± 0.6	65.5 ± 0.6**

*-$P < 0.0001$ vs c-CKD-HTN; **-$P < 0.0001$ vs c-HTN

Keywords: Heart rate; Chronic kidney disease; Hypertension

PO-237

ANALYSIS OF LEFT VENTRICULAR FUNCTION AND OF CORONARY CIRCULATION IN RELATIONSHIP TO RENAL FUNCTION

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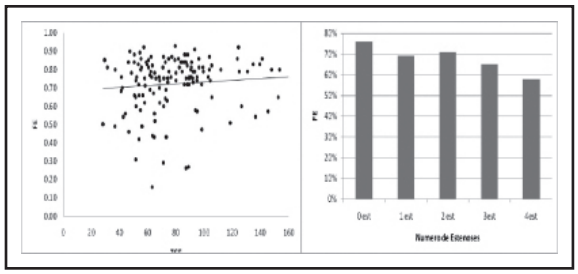
Introduction and Aims: Glomerular filtration rate (GFR) constitutes an important risk factor in cardiovascular disease. Initial GFR reductions greatly increase morbimortality in patients with chronic kidney disease (CKD). Even in the early stages of CKD, it is possible to detect an increase of fatal and non-fatal events related to the cardiovascular system.

To verify if GFR modifications influence the number of coronary vessels having atherosclerotic lesions and to analyze its interactions with left ventricular function (Ejection factor – EF)

Methods: Thus, a study was performed on 142 patients who were sent to the hemodynamic center for angiographic study because they had been suspected of having coronary disease. These patients were divided into three groups according to the patients' GFR which was obtained by the estimated clearance of creatinine (Cockroft Gault). Group 1: (GFR > 90 mL/min), n = 46, average age 53.2 9.10 years (21 females and 25 males). Group 2: (GFR between 60 and 89 mL/min), n = 57, average age 61.7 10.06 (29 females and 28 males). Group 3: (GFR between 15 and 59 mL/min), n = 39, average age 69.5 8.46 (16 females and 23 males). Coronary stenoses were taken into consideration when >60% and scored from 0 to 4, according to the number of vessels affected. Ejection fraction (EF) was determined through the use of left ventriculography which was performed during cardiac catheterization.

Results: Group 1 = 0.86 stenoses/pct, group 2 = 0.82 stenoses/pct and group 3 = 1.35 stenoses/pct (group1 = group 2: $P = 0.8513$; group 3> group1: $P = 0.0414$ and group 3 >group 2: $P = 0.0262$). Observation manifested that the left ventricular function (EF) was correlated to the number of coronary stenoses ($r = -0.3322$; $P = 0.00005$) and that it was not correlated to GFR ($r = 0.1114$; $P = 0.1873$) (Figure 1).



Keywords: Blood volume; Glomerular filtration rate; Urea; Clearance

PO-238

DISCREPANCIES IN HYPERTENSION CONTROL RATES EVALUATED BY MEANS OF OFFICE BP AND AMBULATORY BP MONITORING IN HYPERTENSIVE PATIENTS WITH AND WITHOUT CHRONIC KIDNEY DISEASE

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Our purpose was to evaluate control rates of hypertension by means of office BP or ambulatory BP monitoring (ABPM) in hypertensive patients with or without chronic kidney disease (CKD).

We evaluated 5321 hypertensive patients from the Spanish Society of Hypertension ABPM Registry. CKD was defined according K/DOQI 2002 guidelines. Glomerular filtration rate was estimated by MDRD formula and urinary albumin excretion was assessed by albumin/creatinine ratio. BP control was defined by an office BP (mean of 2 measurements) <140/90 mm Hg and by a daytime BP on ABPM <135/85 mm Hg or a nighttime BP on ABPM <120/70 mm Hg.

A total of 1506 patients (28.3%, 95% CI 27.1–29.5) had CKD. Office BP control was observed in 18.1% of patients with CKD and in 20.8% of patients without CKD ($P = 0.029$) despite CKD patients were receiving more antihypertensive drugs (mean number per day 2.53 vs 2.20, $P < 0.001$). Control of daytime BP was more than double in patients with or without CKD but similar in both groups (51.9% y 51.6%, $P < 0.0001$ vs office control in both groups, $P = 0.837$ between groups). Control of nighttime BP was lower in CKD patients (35.1% vs 43.6% in CKD-free patients, $P < 0.0001$). We conclude that, in hypertensive patients, CKD conferred a worse office BP control despite of a more intense antihypertensive treatment. Control rate of hypertension was more than double when evaluated by means of ABPM daytime BP and similar in patients with or without CKD. Nevertheless, control of nighttime BP was poorer, and lower in CKD patients. Evaluation of hypertension control in CKD should be implemented with ABPM.

Keywords: Chronic kidney disease; Blood pressure control; Ambulatory blood pressure monitoring; Spanish society hypertension ABPM registry

PO-239

IMPAIRED CORONARY MICROCIRCULATION IS ASSOCIATED WITH INCREASED URINE ALBUMIN EXCRETION IN UNTREATED HYPERTENSIVES

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Coronary flow reserve (CFR) is impaired in patients with essential hypertension. Our aim was to investigate the associations between CFR and cardiac and renal damage in untreated hypertensives.

For this purpose, we studied 21 hypertensive patients (aged 58.2 years, eight males, office BP 150/95 mm Hg) with indications of myocardial ischemia and normal coronary arteries in coronary angiography. CFR was calculated by a 0.014 in. Doppler flow wire (Flowire, Volcano) in the left anterior descending artery in response to bolus intracoronary administration of adenosine (60 μg) as the ratio of hyperemic to basal average peak velocity of the distal vessel. All the participants underwent complete echocardiographic study including left ventricular diastolic function evaluation by means of transmitral flow (E, A, E/A ratio) and tissue Doppler imaging (Em, Am) and determination of albumin to creatinine ratio (ACR) on two non-consecutive morning spot urine samples

Based on a cut-off value of 2.5 for CFR, patients were classified into those with high (n = 9) and low (n = 12) CFR. Hypertensives with low CFR compared to those with high CFR decreased transmitral E/A (0.85 vs 1.12, $P = 0.043$) and Em/Am (0.7 vs 0.95, $P = 0.047$), as well as increased heart rate (79.2 vs 69.3 bpm, $P = 0.032$) and aortic pulse pressure measured during catheterization (76.5 vs 58.8 mm Hg, $P = 0.003$). ACR values were also significantly increased in patients with low compared to those with high CFR (29.1 vs 9 mg/g, $P = 0.007$). CFR was negatively correlated with ACR ($r = -0.458$, $P = 0.047$), aortic pulse pressure ($r = -0.675$, $P = 0.001$) and heart rate ($r = -0.644$, $P = 0.002$) measured during catheterization.

Untreated hypertensives with impaired CFR are characterized by intrarenal vascular damage as reflected by increased urine albumin excretion. These findings further support the existence of a diffuse microcirculatory dysfunction in this setting.

Keywords: Microcirculation; Hypertension

PO-240

ASSOCIATIONS OF RENAL HEMODYNAMICS WITH TARGET ORGAN DAMAGE IN UNTREATED HYPERTENSIVES. AN INVASIVE APPROACH

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Measurement of renal resistive index (RRI) in renal arteries has been used to assess the severity of target organ damage in hypertension. Coronary flow reserve (CFR) is often used to express coronary microvascular function and asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase, is a marker of endothelial dysfunction. The aim of the present study was to evaluate the relationship of renal hemodynamics with coronary microcirculation, endothelial function and kidney damage in untreated patients with essential hypertension.

For this purpose, we studied 24 hypertensive patients (aged 57.7 years, 10 males) with indications of myocardial ischemia and normal coronary and renal arteries in the coronary and renal angiography. Renal blood flow velocity was measured by a 0.014 in. Doppler flow wire (Flowire, Volcano) in the renal artery. RRI was calculated as: (peak systolic velocity – end-diastolic velocity)/peak systolic velocity. CFR was calculated by using also Flowire in response to bolus intracoronary administration of adenosine (60 μg). Serum creatinine levels (sCr), glomerular filtration rate (eGFR according to MDRD formula) and ADMA were assessed from a morning blood sample. Albumin excretion was determined as the ratio of albumin to creatinine (ACR) on two non-consecutive morning spot urine samples.

In the entire study population RRI was negatively correlated with CFR ($r = -0.530$, $P = 0.008$) while no correlation was observed with age, sex, anthropometric the renal artery. Moreover, RRI was positively correlated with ADMA ($r = 0.570$, $P = 0.006$), logACR ($r = 0.410$, $P = 0.046$) and eGFR ($r = -0.423$, $P = 0.040$).

Increased vascular resistance of the renal arteries is associated with impaired coronary microcirculation (both assessed invasively), endothelial dysfunction and intrarenal damage (as reflected by increased ADMA levels and albumin excretion, as well as reduced eGFR). RRI may be considered a useful hypertensive target organ damage surrogate.

Keywords: Coronary flow reserve; Renal hemodynamics; Endothelial dysfunction; Albuminuria

PO-241

ALBUMINURIA IS RELATED TO CIRCULATING SOLUBLE RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS AND BIOMARKERS OF ENDOTHELIAL FUNCTION IN HYPERTENSION

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The soluble receptor for advanced glycation end-products (sRAGE) participates in the development and acceleration of atherosclerosis, while albuminuria, L-arginine and asymmetric dimethylarginine (ADMA) are related with vascular dysfunction. In this study we estimated the relationship of albumin to creatinine ratio (ACR) with sRAGE, ADMA and L-arginine in essential hypertensives.

Our population consisted of 180 newly diagnosed untreated non-diabetic patients with stage I–II essential hypertension [102 men, mean age = 53 years, office blood pressure (BP) = 146/94 mm Hg]. According to the ACR values determined as the mean of two non-consecutive morning spot urine samples, the study population was divided into microalbuminurics (n = 32) (mean ACR = 30–300 mg/g) and normoalbuminurics (n = 148) (mean ACR <30 mg/g).

Microalbuminurics compared to normoalbuminurics were had higher 24-hour systolic BP (142 ± 11 vs 131 ± 9 mm Hg, $P = 0.001$), while did not differ regarding metabolic profile (P = NS). Moreover, microalbuminurics compared to normoalbuminurics exhibited lower levels of sRAGE (1012 ± 453 vs 1501 ± 578 pg/mL, $P = 0.003$) and higher levels of ADMA (0.58 ± 0.04 vs 0.43 ± 0.05 μmol/l, $P < 0.0001$) and L-arginine (105 ± 5.6 vs 86 ± 7.3 μmol/L, $P < 0.0001$). In the total population, ACR was positively related to 24-hour systolic BP ($r = 0.415$, $P < 0.0001$), ADMA ($r = 0.324$, $P = 0.01$) and L-arginine ($r = 0.248$, $P = 0.03$), whereas it was negatively

correlated with sRAGE ($r = -0.274$, $P = 0.019$). Regarding sRAGE, it was associated with 24-hour pulse pressure ($r = -0.365$, $P = 0.001$) and ADMA ($r = -0.225$, $P = 0.002$). Multiple regression analysis revealed that age, 24-hour systolic BP, sRAGE and ADMA were the independent predictors of ACR ($R^2 = 0.52$, $P < 0.0001$).

In essential hypertensives, microalbuminuria is accompanied by attenuated levels of sRAGE and augmented ADMA and L-arginine reflecting pronounced vascular dysfunction. Moreover, the association of ACR with sRAGE and ADMA, further supports the integrative role of albuminuria in hypertension.

Keywords: Albuminuria; Kidney; Atheroslerosis; Endothelium

PO-242

CHRONIC KIDNEY DISEASE EDUCATION IN THE COMMUNITY HEALTH CENTER SETTING IMPROVES PRESCRIPTION FILLING RATES FOR ANTIHYPERTENSIVE MEDICATIONS

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Background: Hypertension is one of the most prominent health problems in the United States. According to the CDC, 30% of adults are hypertensive, and 25% are pre-hypertensive. Hypertension is a leading risk factor for Chronic Kidney Disease (CKD); thus, hypertension control is critical for preventing CKD, among other complications. Low-income and minority patients are at increased risk for hypertension – indicating the need for strategic efforts targeting hypertension control among this population. We hypothesize that an educational intervention addressing hypertension control, a key component of CKD prevention and management, among primary care providers serving in a community health center (CHC) will result in improved patient management.

Methods: A CHC was selected for an educational intervention addressing hypertension management, among other risk factors for CKD. Nephrologists from a regional academic medical center conducted educational sessions addressing national guidelines for hypertension and CKD management with clinic providers and staff. Site visits were conducted weekly for 6-months and were tapered over a 3-year period. Electronic pharmacy records were queried for data on antihypertensive medication prescriptions for the pre-intervention and maintenance phases. Descriptive statistics were used to highlight trends in prescription filling over 3 years. Paired sample *t*-tests were used to compare the mean filling rates between the pre-intervention and maintenance phases.

Results: Preliminary data indicate a statistically significant increase (mean increase = 27%) in prescriptions for antihypertensive medications. Further analysis is needed to determine the impact of confounding factors on the selected outcome measure. Additionally, a sub-study of changes in individual blood pressure management during the study period is underway.

Discussion: Results from this study indicate that offering continuing hypertension education to providers in CHCs may improve management of high-risk patients, thereby preventing associated complications.

Keywords: Hypertension education; Community health centers; High risk; Primary care

Off-Target Cardiovascular Effects of Non-Cardiovascular Drugs

PO-243

SITAGLIPTIN IS ASSOCIATED WITH INCREASED BLOOD PRESSURE IN RATS

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Introduction: Sitagliptin is a DPP-4 inhibitor with positive effects on blood glucose that was approved for treatment of diabetes. However, data on the additional effects of the drug on the vasculature is lacking. We studied the effects of DPP-4 inhibition on vascular disease in a metabolic syndrome model of fructose fed rats.

Methods: Twenty four 8 week old male Spargue–Dawly rats were divided into four groups. Two groups were fed chow (CFR), and two groups were fed a high fructose diet (FFR), which means that 50% of the calories will originate from Fructose in diet. One group of the FFR and one of the CFR were given Sitagliptin 20 mg/kg/day in drinking water. Blood pressure, body weight and food intake were measured weekly.

Results: Hi fructose diet increased blood pressure from 110 to 150 mm Hg, In fructose fed rats sitagliptin improved lipids with no effect on blood pressure. In Chow fed rats sitagliptin increased blood pressure and had no effect on lipids. Regardless of diet sitagliptin increased media to lumen ratio of aorta.

Keywords: Hypertension; Sitagliptin; Rat

PO-244

BLOOD PRESSURE EVALUATION IN ONCOLOGY AND CNS INDICATIONS: IMPLEMENTATION OF ABPM AND HOME BP TELEMONITORING

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Within the drug development research arena, there is an increasing focus on defining the blood pressure response from a cardiac safety (vs efficacy) persepctive. The evaluation of a blood pressure repsonse outside of hypertension research, requires a unique approach to evaluating the blood pressure response from early phase to late phase clinical development/trials.

The goal of this presentation is to: 1. Provide insight into the methodology and approach to defining a blood pressure repsonse from a safety perspective for indications outside of hypertension.
2. Review the benefits and challenges to the implementation of specific BP technologies in a therapeutic indication outside of hypertension.
3. Provide case studies within Oncology and CNS indications, including preliminary data from (2) trials that incorporated either ABPM and telememonitoring or telemonitoring home BP as a stand alone BP evaluation methodology.

Perspective will be provided from a regulatory, clinical and drug development perspective.

Keywords: Blood pressure response; Oncology; CNS; ABPM and telemedicine in clinical research

Poster Session III
Arterial Structure and Compliance

PO-245

VASCULAR INJURY IN HYPERTENSIVE PATIENTS. ARE MEN AND WOMEN EQUAL? PARITE STUDY

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To describe complementary examinations undertaken to identify target organ injury in patients with essential hypertension as a function of gender and cardiovascular risk (CVR).

Cross-sectional, multicentric study conducted in France with 654 cardiologists, each of whom included four consecutive, gender-paired patients with hypertension for whom details of complementary examinations carried out over the last 6 months were available.

Three thousand four hundred and forty patients included (53% M, 47% F); F were older than M, 67.3 years ± (12) vs 64.6 years ± (12). Examinations: echocardiography 66.2%; vascular Doppler 40.2%; coronary ischemia testing 34%; Holter EKG 14.1%.

Significant differences between M and F were found in terms of the examinations undertaken. Myocardial ischemia testing was significantly more frequent in M than F, particularly when CVR was medium or high.

Tests to identify coronary insufficiency are performed more often in men with hypertension than in women with hypertension. This difference is observed for identical CVR. As in other fields, efforts to promote parity should probably be encouraged.

Table I.

Examination	Females	Males	*P*
Standard echocardiography or TOE %	65.8	66.5	0.69
Exercise test ET %	18.8	40.7	<0.001
Ischemia test without ET–no ET- %	5.9	8.2	0.007
Vascular Doppler %	36.9	43.2	<0.001
Ischemia testing (ET + no ET)			
Low CVR (n), %	(81), 21.0	(20), 15.0	0.76
Medium CVR (n), %	(528), 14.4	(441), 30.4	<0.001
High CVR (n), %	(1012), 26.9	(1358), 49.1	<0.001

Keywords: Vascular injury; Essentiel hypertension; Gender; Cardiovascular risk

PO-246

PERIPHERAL PULSE PRESSURE STRONGLY CORRELATES WITH CENTRAL SYSTOLIC BLOOD PRESSURE IN ADULTS: BOGALUSA HEART STUDY

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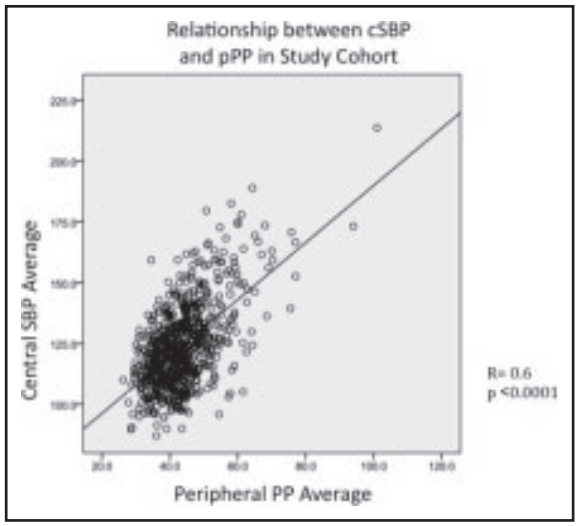
Introduction: Aortic stiffening causes early pulse wave reflection, increased augmentation pressures, and ultimately increased central systolic blood pressure (cSBP). Measurements of aortic compliance are important predictors of cardiovascular mortality; however, the relationship between central parameters and peripheral parameters has not been fully described. This study sought to examine the relationship between cSBP and peripheral pulse pressure (pPP).



Methods: Participants underwent four blood pressure measurements with a standard cuff and four applanation tonometry measurements with an Omron device. All measurements were performed on the subject's right arm in a sitting and rested position.

Results: We compared pPP with cSBP in 705 participants from the Bogalusa Heart Study. Participants were 30.4% black, 69.6% white and 40.6% were male (mean age of 43.3 years ± 4.4). Overall, linear regression showed strong correlation between pPP and cSBP ($R = 0.6$; $P < 0.001$). Correlation remained strong when the cohort was divided by race (blacks: $R = 0.62$; $P < 0.001$, whites: $R = 0.5$; $P < 0.001$) and sex (males: $R = 0.52$; $P < 0.001$, females: $R = 0.63$; $P < 0.001$) (Figure 1)

Discussion: Peripheral PP and cSBP were strongly correlated, suggesting increased aortic stiffening is associated with predictable increases in pPP. While all race and sex groups showed a significant correlation between pPP and cSBP, our data suggest females and blacks may be more represented by the relationship than white males. Changes in pPP therefore may provide insight into the degree of aortic stiffening when assessing cardiovascular risk and response to hypertensive treatment.

Pearson *R* Values

	Whites	Blacks	Total
Men	0.40	0.60	0.52
Women	0.56	0.65	0.63
Total	0.50	0.62	0.60

Keywords: Bogalusa heart study; Aortic compliance; Pulse pressure; Non-invasive monitoring

PO-247

ADDITION OF EPLERENONE TO RAAS BLOCKADE IN PATIENTS WITH CKD AND PROTEINURIA CORRELATES WITH BASELINE VASCULAR COMPLIANCE

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Chronic kidney disease (CKD), proteinuria and increased arterial stiffness are associated with increased cardiovascular disease risk. We performed a prospective randomized trial of subjects with stage 1–3 CKD and proteinuria >500 mg/day. All subjects were on RAAS blockade with either an ACE or ARB prior to enrollment. Subjects were then randomized to 3 treatment groups in addition to their current treatment: group 1- ACE + ARB, 2- ACE/ARB + eplerenone, 3- ACE/ARB + isosorbide mononitrate. Subjects were followed for 4 months and had pulse wave velocity (PWV) and central pulse pressure (CPP) measured (SphygmoCor PV device] at baseline and after 4 months of randomized drug therapy.

Results: Thirty-four subjects were randomized to the study (mean age = 53.9 ± 13.6 years; males (82%); mean GFR = 54.7 ± 25.7 mL/min/1.73 m^2). There were 2 drop outs in group 1. Proteinuria decreased in group 1 and 2 but increased with the addition of the nitrate in group 3. BP declined similarly in all 3 groups over the treatment period. Urine protein excretion (g/day) was reduced by 0.32 ± 0.2 in group 1, 1.04 ± 0.4 in group 2, −0.2 ± 0.3 in group 3. The correlation between baseline values of PWV, brachial pulse pressure (BPP), CPP with the change in urine protein excretion by treatment group as shown in the Table below.

Conclusion: There was a significant correlation between baseline arterial stiffness as measured by aortic PWV and a decrease in proteinuria in subjects receiving RAAS blockade when combined with eplerenone. The mechanism of antiproteinuric effect of mineralocorticoid blockade may be more related to factors that promote fibrosis (and thus increased PWV) when compared with dual RAAS blockade or nitrate use which may depend more on direct hemodynamic changes.

	PWV	BPP	CPP
Group 1 (n = 7)	$r = 0.35$, $P = 0.65$	$r = -0.2$, $P = 0.8$	$r = -0.1$, $P = 0.8$
Group 2 (n = 14)	$r = 0.6$, $P = 0.02^*$	$r = 0.2$, $P = 0.5$	$r = 0.3$, $P = 0.4$
Group 3 (n = 13)	$r = -0.6$, $P = 0.09$	$r = -0.13$, $P = 0.7$	$r = 0.1$, $P = 0.8$

Keywords: PWV; Proteinuria; CKD; Vascular compliance

PO-248

ARTERIAL STIFFNESS EVALUATION IN HIV PATIENTS

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Arterial stiffness (AS) is considered an important factor that determines Cardiovascular Diseases. Few studies on evaluation of AS in HIV patients have been publish; most of then concluded that increases in AS in HIV+ patients could be related to the HIV infection per se y subsequent immunosuppression more than the traditional Cardiovascular Risk Factors. The aim of the study was to evaluate AS in HIV+ patients. Thirty-six HIV+ patients were evaluated (nine females, 27 males, age 36 ± 10 years.). Ninety-three subjects (45 females, 48 males, age 40.7 ± 11 years.) were used as a control group. BrachialBP (SBP, DBP) and AS (Systemic Vascular Compliance [SVC], Brachial Artery Compliance [BAC] and Distensibility [BAD]) were obtained using a noninvasive transducer (DynaPulse200M) for pulse waveform analysis. Comparison were made using independent *t*-test, and level of significance of $P < 0.05$.

Results: anthropometric characteristics are shown in Table. SVC (1.19 ± 0.17 vs 1.53 ± 0.26 mL/mm Hg, $P = 0.000$), BAC (0.067 ± 0.02 vs 0.083 ± 0.03 mL/mm Hg, $P = 0.000$) and BAD (6.099 ± 1.01 vs 7.043 ± 1.26%/mm Hg, $P = 0.000$) were statistically lower in HIV+ patients than in the control group. AS parameters (SVC, BAC, BAD) did not show correlation with age, weight or CD4+ cell count. Different biological markers should be study to further understand the development of Arterial stiffness in HIV patients.

Table I. Anthropometric characteristics

	HIV+ patients	Control group	*P*
Age (years)	36.0 ± 10.1	40.7 ± 11.6	0.036
Weight (kg)	67.2 ± 10.4	77.6 ± 17.9	0.001
Height (cm)	165.9 ± 9.6	166.6 ± 9.6	0.721
SBP (mm Hg)	115.7 ± 13.4	115.8 ± 9.2	0.979
DBP (mm Hg)	68.9 ± 9.3	76.2 ± 7.5	0.000
HR (bbm)	77.8 ± 13.9	73.9 ± 11.8	0.115

Keywords: Arterial stiffness; HIV; Systemic vascular compliance; Brachial artery compliance

PO-249

A NEW VIBRATIONAL APPROACH FOR CAROTID PULSE WAVE VELOCITY ASSESSMENT

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Objective: Arterial stiffness is a key parameter in evaluating vascular health. When locally evaluated at carotid site, it well correlates with the stage of degenerative atherosclerotic process and it could be considered an useful indicator of global cardiovascular risk.

At the present, the state-of-the-art methods for evaluation of local carotid stiffness are based on the analysis of vascular distensibility and local tonometry.

Aim of this work is to introduce a new system for local carotid pulse wave velocity (PWV) assessment based on the evaluation of the vibrations locally induced by the propagation of the arterial pulse pressure.

Design and Methods: Eight young healthy subjects (28.4 ± 2.1 years, 62.5% males, BMI 21.6 ± 2.14 kg/m^2) have been recruited. Two percutaneous accelerometers were placed on the neck of each subject few centimetres apart along a straight segment of the common carotid artery. The accelerometric signals were acquired and processed beat-to-beat in order to obtain the temporal value (i.e. pulse transit time, PTT) at which the maximal degree of similarity between them was obtained. In particular, ad-hoc fiducial points have been chosen, allowing an optimal signal alignment.

Results: The mean PWV, calculated from the distance (mean 3.81 ± 0.58 cm) between the position of the two accelerometers

and the PTT, was 3.16 ± 1.09 m/s, a reasonable value for elastic artery of young people.

Conclusions: In conclusion, a new cheap, easy-to-use and non-invasive system for local carotid pulse wave velocity assessment based on the analysis of local vibrations is proposed. For its characteristics it might be considered as a valid alternative to available approaches.

Keywords: Stiffness; Pulse wave velocity; Carotid; Compliance

PO-250

CENTRAL-PERIPHERAL BLOOD PRESSURE DIFFERENCES ARE GREATER IN HISPANICS AND AFRICAN-AMERICANS

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Increased arterial wave reflection is associated with elevated central pressure, which better predicts CV events compared to peripheral pressure although peripheral pressure is commonly used. African-American (AA) and Hispanic (H) populations have higher rates of CV events compared to Caucasians (C), although there is no difference in peripheral blood pressure guidelines. Arterial Applanation tonometry is used to measure wave reflection and central pressures. We evaluated the association between central and peripheral pressures and wave reflection among healthy AA, H and C subjects.

We studied 93 healthy volunteers, 30% C, 37% AA, 33% H (age 40 ± 11 years). Peripheral systolic blood pressure (PSBP) was measured using an automated sphygmomanometer device. Central systolic blood pressure (CSBP), augmented pressure (AP) which is the magnitude of the reflected wave, and heart rate corrected augmentation index (AI75) were derived from radial artery applanation tonometry using a transfer function (Sphygmocor®, Atcor Medical). Comparisons were made between the groups using independent *t* test and ANOVA. Linear regression was used for multivariate relations.

Height, weight, BMI, age, PSBP, diastolic and pulse pressure were similar between the three groups. AA had higher CSBP compared to C (114 ± 19 vs 104 ± 8 mm Hg, $P = 0.025$). On ANOVA there was a trend toward a higher CSBP in the C, H and AA groups (104 ± 8 vs 110 ± 18 vs 114 ± 19, $P = 0.08$) respectively. AP was higher in AA and H subjects (8 ± 5 vs 4 ± 5 mm Hg, $P = 0.002$) and (6 ± 4 vs 4 ± 5 mm Hg, $P = 0.05$) respectively. Similarly, AI75 was higher in AA and H subjects (19 ± 10 vs 6 ± 12%, $P < 0.001$) and (15 ± 11 vs 6 ± 12%, $P = 0.001$) respectively. On multivariate analysis adjusted for age, gender, height, and mean arterial pressure, only age, female gender, AA and H ethnicity were associated with a significantly higher augmentation index ($R^2 = 0.48$, $P < 0.001$).

These results demonstrate ethnic differences in wave reflection and CSBP despite similar peripheral pressures. Compared to C, AA and H have significantly greater wave reflection that may in part account for higher central systolic pressure and the higher prevalence of CV events in these groups. Measurement of peripheral pressures alone may underestimate the central vascular burden of hypertension in different ethnicities.

Keywords: Arterial stiffness; Central pressure; Ethenicity

PO-251

THE LEFT VENTRICULAR SEPTAL – AORTIC ANGLE RELATIONSHIP WITH THE AUGMENTATION INDEX AND CENTRAL BLOOD PRESSURES

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The left ventricular (LV) septal – aortic angle increases with age, which may result in the basal ventricular septum protruding into the LV outflow tract (OT), sometimes associated with basal septal hypertrophy and called a "septal bulge." This has been shown to increase the LVOT blood velocity and pressure gradient. The reflected pressure wave is known to be affected by LV ejection dynamics. Additionally, whether the septal bulge is a consequence of aging or blood pressure (BP) is unclear. Arterial stiffness is known to impact left LV hypertrophy. We therefore hypothesized that the aortic angle may be related to the reflected pressure wave and augmentation index (AI). We studied 135 subjects (age 58 ± 16 years) that had echocardiograms and radial artery applanation tonometry. Thirty-five percent were male. Central systolic BP (CSBP), augmented pressure (AP), and AI were derived from applanation tonometry and a validated transfer function (Sphygmocor®, Atcor Medical). AI was corrected for heart rate (AI75). The end-systolic angle (ESA) and end-diastolic angle (EDA) between the right septal surface and anterior aortic wall was measured using the parasternal long axis echocardiographic view.

Mean ESA was 118 ± 11 and mean EDA was 112 ± 13. Mean AI75 was 21 ± 12. On univariate analysis the ESA, but not EDA, correlated with AI75 ($r = -0.22$, $P = 0.01$), AP ($r = -0.27$, $P = 0.02$), CSP ($r = -0.21$, $P = 0.02$), CPP ($r = -0.24$, $P = 0.006$) and PPA ($r = 0.26$, $P = 0.005$). ESA did not correlate with PSBP ($r = -0.15$, $P = 0.10$) or PPP ($r = -0.14$, $P = 0.14$). Multivariate analysis corrected for age, gender, height, cardiovascular risk factors, and mean arterial pressure demonstrated AI75 to be an independent predictor of ESA (B = −0.18, $P = 0.048$). Our results suggest that a narrower systolic LV – aortic angle may be associated with a greater reflected pressure wave and higher central BP.

Keywords: Arterial stiffness; Central blood pressure; Left ventricular outflow tract obstruction

PO-252

DIFFERENCES IN POST-ISCHEMIC REACTIVE HYPEREMIA TISSUE OXYGEN SATURATION BETWEEN NORMALS AND HYPERTENSIVE SUBJECTS

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Endothelial dysfunction is an early step in the development of atherosclerosis and has prognostic value in a variety of disease states. Large artery endothelial function is commonly assessed by the change in brachial artery dimension post hyperemia using ultrasound. Methodologies to evaluate microcirculatory vascular function are less available. Tissue oxygen saturation (StO2) derived from near-infrared spectroscopy (NIRS) is a measure of tissue perfusion and StO2 changes represent regional oxygen delivery. Post-ischemic reactive hyperemia StO2 changes have been used to assess peripheral vascular disease. StO2 values also are predictive of adverse outcomes in heart failure.

We hypothesized that microcirculatory function and oxygen delivery can be evaluated and may differ in hypertensive (HTN) and normal (NL) subjects. Our objective was to compare changes in microcirculatory flow in HTN and NL subjects using StO2 changes with the provocative maneuver of hyperemia.
The study population consisted of 21 NL and 22 HTN subjects. The NL group was younger (30 ± 7 vs 59 ± 13, $P < 0.001$). StO2 was measured in the thenar eminence of the hand using the Inspectra Oxygenation NIRS Monitor (Hutchinson Technology). StO2 parameters measured at rest and post 5 minutes brachial artery ischemia included baseline StO2, occlusion slope (OS), slope of recovery (RS). Baseline StO2 (86.6 ± 4.0 vs 85.3 ± 5.6, $P = 0.31$) was similar between the NL and HTN groups. The OS (-8.9 ± 2.0 vs -6.3 ± 1.5, $P < 0.001$) and RS (4.4 ± 1.3 vs 3.3 ± 0.99, $P = 0.003$) were significantly different. On linear regression analysis only HTN was an independent predictor of OS, while age predicted RS.
Alterations in StO2 OS to reactive hyperemia are different between HTN and NL. These changes may be useful in evaluating microcirculatory dysfunction.

Keywords: Microvascular function; Reactive hyperemia; Arterial stiffness

PO-253

THE RELATIONSHIP BETWEEN IMPAIRED LUNG FUNCTION AND CARDIAC FUNCTION IN OLDER INDIVIDUALS

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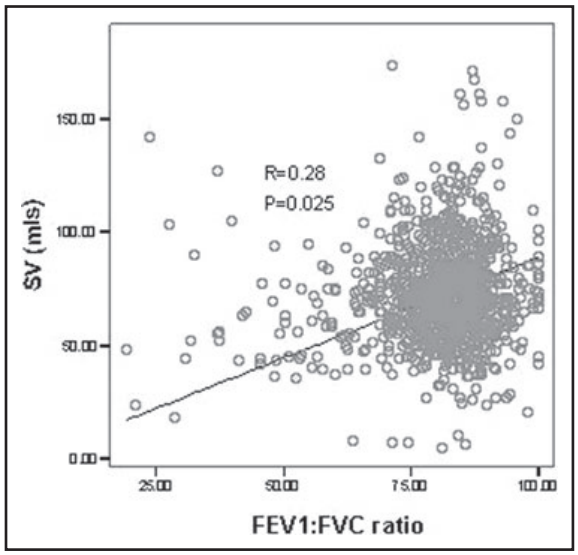
Background: Impaired lung function is associated with increased cardiovascular (CV) risk although the underlying mechanisms remain unclear. We have previously shown that lung function is inversely related to arterial stiffness in older men, and that patients with chronic obstructive pulmonary disease (COPD) have increased arterial stiffness. Furthermore, arterial stiffness is associated with impaired diastolic function in individuals with COPD. Our aim was therefore to examine the relationship between cardiac function and lung function in a population-based cross-sectional study

Methods: Data from 1026 individuals, aged between 50 and 92 years, from the Anglo Cardiff Collaborative Trial, were available for the current analyses.
Peripheral blood pressure was recorded (Omron 711) in the supine position according to BHS guidelines.
Cardiac function was assessed by measuring stroke volume (SV), using a non-invasive, inert gas re-breathing technique (InnoCor, Innovision A/S, Denmark).
Spirometry was performed (Vitalograph) to assess the degree of airways obstruction by measuring forced expiratory volume in 1 second: forced vital capacity ratio (FEV1:FVC).

Results: After entering all confounding factors of FEV1:FVC ratio (age, height, gender, smoking status, body surface area, heart rate, peripheral vascular resistance and mean arterial pressure) into a stepwise multivariate linear regression model, SV remained independently related to lung function ($R = 0.28$, $P = 0.025$) (Figure 1).

Conclusions: Stroke volume is independently associated with impaired lung function in this population based study, suggesting a mechanism whereby impaired lung function may increase CV risk. Increased arterial stiffness, which is associated with impaired lung function, may be an important mechanism mediating the relationship between cardiac function and lung function.



Keywords: Lung function; Cardiac function; Stroke volume; Large artery stiffness

PO-254

HYPEREMIA INDUCED CHANGES IN CAROTID-RADIAL PULSE WAVE VELOCITY BEFORE AND AFTER PRE AND POST ISCHEMIC CONDITIONING

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Brief repeated episodes of ischemia prevent the ischemic complications of cardiovascular events when applied before (pre) or after (post) an event. This phenomenon (known as conditioning) can be induced by a variety of techniques. Although a number of studies have evaluated the effects of conditioning using clinical endpoints, more sensitive techniques by which measure its effects are lacking. Hyperemia induced dilation of the brachial artery using ultrasound has been proposed to assess the effects of pre and post ischemic conditioning. Since hyperemia decreases carotid to radial pulse wave velocity (PWV), we sought to determine whether hyperemia changes (Δ) in PWV could be used to assess the effects of pre and post conditioning. We studied the effects of hyperemia induced by release of arterial cuff occlusion before and after prolonged (7.5 minutes) ipsilateral arm ischemia in 20 healthy subjects, 71% male 31 ± 9 years. The protocol was repeated on two separate days using pre and post conditioning stimuli (3 × 30 seconds contralateral arm occlusions). Hyperemia resulted in an 8.6% decrease ($P = 0.02$) in PWV before but not after prolonged ischemia (-1.2%, $P = 0.38$). Induction of a pre-ischemic stimulus restored the PWV decline to 13% ($P = 0.003$) in 10 subjects and a post ischemic stimulus restored the PWV decline to 7.6% ($P = 0.02$) in 15 subjects. In conclusion, prolonged ipsilateral ischemia blunts the normal PWV decline produced by hyperemia. Induction of contralateral conditioning stimuli restored this response. This technique may be useful for the assessment of novel treatment strategies that employ pre and post ischemic conditioning in protecting the cardiovascular system.

Keywords: Ischemic conditioning; Pulse wave velocity; Arterial function

PO-255

THE PREDICTIVE VALUE OF CAROTID ARTERY FEATURES OVER TRADITIONAL RISK FACTORS AND ENDOTHELIAL FUNCTION

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Vascular abnormalities are present from early stages in chronic kidney disease (CKD) patients with multiple risk factors as diabetes and hypertension. The therapeutic strategies to prevent progressive cardiovascular disease should be initiated early and vascular integrity and function closely monitored.

We have studied common carotid intima media thickness (CIMT), internal carotid plaque and stenosis and assessed endothelial function by brachial flow mediated dilatation (FMD) in CKD and end stage renal disease (ESRD) patients. After 1 year we have evaluated the prediction power of cardiovascular risk factors for end point events and compared the predictive value of carotid artery features and endothelial function.

Doppler examinations were performed on 67 patients with renal disease and 26 healthy matched controls. FMD was tested on 86 subjects. CIMT and FMD on CKD or ESRD have been significantly different vs controls and in strong inverse correlation (r 0.8, P 0.001). Blood pressure has been different between groups (P 0.000 and 0.048). Ten yearly end point events have been present on patients with one or more of the following carotid features: stenosis, plaque, or IMT over 75 percentile. All hemodialysis (HD) patients that have reached an end point presented endothelial dysfunction irreversibility after one dialysis session. Changes in FMD after HD correlated with CIMT measurements (r 0.5, P 0.001).

The end point events prediction was evaluated with an original artificial neural networks (ANN) classifier. This has utilized all 93 subjects data as input: 24 risk factors known, including the traditional and noninvasive markers (P1) and repeated without carotid plaque/stenosis markers (P2) or without structural carotid markers and diabetes (P3) by retraining the components which contribute more than 0.0001. Success rate prediction is greatly enhanced by utilizing the carotid structural markers independent of diabetes presence: P1 = 0.8125, vs P2 = 0.5 and P3 = 0.625. Extrapolating, FMD prediction was only 0.7689.

In conclusion, a new ANN approach to cardiovascular outcome prediction in renal disease, improves greatly with carotid artery features assessment which outstages traditional risk factors and endothelial function. FMD test is important in assessing endothelial function modification produced by the HD treatment. The information obtained from its use as predictor for end point events is surpassed by the carotid markers.

Keywords: Endothelial function; Carotid features; Renal disease; Risk stratification

PO-256

DETERMINANTS OF CENTRAL REFLECTED PRESSURE WAVES

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Background: Central reflected pressure waves can be characterized by arrival time (Tr), believed to be determined by pulse wave velocity (PWV), and amplitude, most closely related to the whole-body reflection coefficient. We investigated the contribution of arterial stiffness (carotid-femoral PWV) to central augmentation index (AI) and also assessed whether systemic vascular resistance (SVR, determined principally by distal arteriolar constriction and a likely surrogate for the reflection coefficient), is also related to AI.

Methods: Arterial wave parameters were estimated from radial arterial tonometry in a convenience sample of 240 individuals; smaller samples were available for PWV (Colin VP2000, n = 51) and SVR (impedance cardiography, BioZ, n = 79). Data are expressed as [mean (SD), range].

Results: A wide range of values for age [43.4 (18), 16–82 years], systolic blood pressure [SBP = 129 (34), 87–218 mm Hg], heart rate [66.7 (12.7), 44–102], PWV [9.2 (3.3), 5.9–21.5 m/s], and SVR [1288 (403), 668-2528 dynes-sec-cm^5] was included. The Table I shows data for Tr (foot of reflected wave, ms), T2 (peak of reflected wave, ms), ED (ejection duration, ms) and AI (% of central pulse pressure).

PWV did not correlate well with Tr ($r = -0.20$, $P = 0.18$) or T2 ($r = -0.47$, $P = 0.741$) but did correlate well with AI ($r = 0.55$, $P < 0.001$). SVR was correlated with Tr ($r = -0.38$, $P = 0.001$) and T2 ($r = -0.008$, $P = 0.94$) and also with AI ($r = 0.58$, $P < 0.001$). Neither Tr nor T2 correlated significantly with HR or ED; HR was unrelated to ED.

Conclusions: The magnitude of wave reflection (AI) is determined both by arterial stiffness (PWV) and arteriolar constriction (SVR) and thus depends on large and small artery characteristics. However, the variation in reflected wave timing is very small (i.e. Tr and T2 are relatively fixed in late systole) and thus PWV has a limited impact on AI. Because the timing of the reflected wave is relatively constant and independent of age, blood pressure or heart rate. The reflected wave may be a conserved parameter.

Table I.

Variable	Mean	SD	Min	Max
Tr	145	24.2	96	266
T2	215.2	33.5	149	274
ED	312	31.9	186	391
AI	128.5	33.01	70	256

SD, standard deviation; Min, minimum value; Max, maximum value; ED = ejection duration.

Keywords: Augmentation index; Pulse wave velocity; Systemic resisitance

PO-257

REGULAR EXERCISE-INDUCED UPREGULATION OF CIRCULATING ENDOTHELIAL PROGENITOR CELLS ATTENUATES AGE-RELATED DECLINE IN ARTERIAL ELASTICITY IN HEALTHY MEN

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Deficiency in number and activity of circulating EPCs is associated with reduced arterial elasticity in humans with advancing aging. Physical exercise can increase the number and activity of circulating EPCs in humans. Here we investigated whether regular exercise-induced upregulation of circulating endothelial progenitor cells (EPCs) improves age-related decline in arterial elasticity in healthy men. In a cross-sectional study, the number and activity of circulating EPCs as well as brachial-ankle pulse wave velocity (baPWV) of young and older sedentary or endurance-trained healthy men were studied. Then we observed the effect of regular exercise on circulating EPCs and baPWV of 10 older and 10 young sedentary healthy men. In both sedentary

and endurance-trained men, the number and activity of circulating EPCs was significantly low in older men compared with young men, which was paralleled to increased baPWV. After 3 months of regular exercise, the number and activity of circulating EPCs increased, and the baPWV of 10 older and 10 young sedentary healthy men decreased. However, the upregulation of circulating EPCs and decreased baPWV of older sedentary healthy men was higher. There was a close correlation between circulating EPCs and baPWV. Multivariate analysis identified proliferative activity of circulating EPCs as an independent predictor of baPWV. The present study demonstrates for the first time that regular physical exercise-induced upregulation of circulating EPCs attenuates age-related reduction in arterial elasticity in healthy men. These findings provide novel insights into the protective effects of exercise on age-related vascular injury.

Keywords: Endothelial progenitor cells; Arterial elasticity; Exercise; Endothelium

PO-258

SUBENDOCARDIAL VIABILITY RATIO AS AN INDEX OF IMPAIRED CORONARY FLOW RESERVE IN UNTREATED HYPERTENSIVES

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Coronary flow reserve (CFR) is the magnitude of the increase in coronary flow that can be achieved in going from basal coronary perfusion to maximal coronary vasodilatation and is often used to express coronary microvascular function. Subendocardial viability ratio (SEVR), calculated through pulse wave analysis, is an index of myocardial oxygen supply and demand. Our aim was to evaluate the relationship between CFR and SEVR in untreated essential hypertensives

We examined 36 consecutive untreated hypertensives (aged 57.9 years, 12 males, all Caucasian) with indications of myocardial ischemia and normal coronary arteries in coronary angiography. CFR was calculated by a 0.014 in. Doppler guidewire (Flowire, Volcano) in response to bolus intracoronary administration of adenosine (60 μg). SEVR was calculated non-invasively by radial applanation tonometry and constitutes a pressure–time integral ratio derived from pressures measured in the aorta and left ventricle. The numerator of the ratio, the diastolic pressure–time integral, is the area between the aortic and left ventricular pressures in diastole and the denominator, the systolic pressure–time integral, is the area under the left ventricular pressure curve in systole. Diastolic function was evaluated by means of transmitral flow and tissue Doppler imaging.

Based on a CFR cut-off value of 2.5 hypertensives were classified into those with normal (n = 12) and low (n = 24) CFR. Hypertensive patients with low CFR compared to those with normal CFR exhibited significantly decreased SEVR by 24.5% ($P = 0.002$). In hypertensives with low CFR, CFR was correlated with SEVR ($r = 0.651$, $P = 0.001$). After applying multivariate linear regression analysis, age, left ventricular mass index, Em/Am, 24 hour diastolic BP and SEVR turned out to be the only independent predictors of CFR (adjusted R square = 0.718).

Estimation of SEVR by using applanation tonometry may provide a reliable tool for the assessment of coronary microcirculation in essential hypertensives with indications of myocardial ischemia and normal coronary arteries.

Keywords: Coronary flow reserve; Pulse wave velocity

PO-259

IMPAIRED CORONARY MICROCIRCULATION IS NOT ACCOMPANIED BY ADVERSE VASCULAR REMODELING IN UNTREATED HYPERTENSIVES

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Hypertension with LVH is associated with both coronary vascular remodeling and attenuated coronary flow reserve. Optical coherence tomography (OCT), in contrast to intravascular ultrasound, can easily identify intimal thickening (IT) from intima-media thickness (IMT). Our aim was to evaluate the relationship between structural and functional alterations of coronary circulation in hypertensives without LVH.

We examined 13 untreated hypertensives (aged 59 years, six males, without echocardiographic-detected LVH) with indications of myocardial ischemia and normal coronary arteries in coronary angiography. CFR was calculated by a 0.014 in. Doppler guidewire in the LAD in response to bolus intracoronary administration of adenosine (60 μg). Fot the OCT study, the image-wire was positioned in the proximal part of the LAD and images at 400-μm intervals were acquired for at least 6 mm vessel length (15 frames). IT was identified as the signal-rich layer nearest the lumen and IMT as the distance from the internal border of this layer to the outer border of the signal-poor middle layer. Accordingly, the average values of maximal IT and IMT of all frames were measured.

Based on a CFR cut-off value of 2.5 hypertensives were classified into those with normal (n = 16) and low (n = 10) CFR. Hypertensive patients with low CFR compared to those with normal CFR exhibited significantly increased aortic systolic BP (159.2 vs 141.6 mm Hg, $P = 0.021$) and pulse pressure measured during catheterization (79.2 vs 59.4 mm Hg, $P = 0.001$). No difference was observed between study subgroups with respect to age, gender and LV mass index (92 vs 84, $P = 0.43$). Hypertensives with low compared to those with normal CFR exhibited significantly decreased vessel area (measured by OCT) (7.8 vs 9.5 mm^2, $P = 0.045$) and average values of maximal IMT (0.28 vs 0.35 mm, $P = 0.035$). Difference in maximal IT was not statistical significant (0.16 vs 0.20 mm, $P = 0.14$). In the entire study population, there was no correlation between IT and IMT with CFR.

In hypertensives without LVH but with indications of myocardial ischemia and normal coronary arteries, impaired coronary microcirculation (based on decreased CFR values) is not accompanied by adverse vascular remodeling (based on OCT imaging).

Keywords: Coronary flow reserve; Optical coherence tomography

Blood Pressure Measurement/Monitoring

PO-260

COMPARISON OF CENTRAL HEMODYNAMICS BETWEEN A_PULSE AND OTHER TWO TONOMETRY-BASED DEVICES

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Our aim was to investigate the accuracy of A_PULSE CASPro®, a new applanation tonometry device, in non-invasive

hemodynamic measurements in comparison with other two tonometry-based devices and evaluate its potential application in clinical practice. Central systolic blood pressure (SBP) and radial augmentation index (AI) were compared between A_PULSE, SphygmoCor and PulsePen, in 34 consecutive patients (59.4 ± 14.1 years) from our ambulatory cardiovascular department. We found no significant interclass difference in central SBP between A_PULSE and SphygmoCor or PulsePen ($P \geq 0.106$), but their absolute difference was significant ($P \leq 0.031$). Particularly, A_PULSE estimated higher aortic SBP than SphygmoCor by 4.7 ± 7.9 mm Hg, and estimated lower aortic SBP by 5.7 ± 6.1 mm Hg, as compared with PulsePen carotid SBP. No significant difference was detected in radial AI when A_PULSE was compared to the other two devices ($P \geq 0.089$). A_PULSE significantly correlated to SphygmoCor and PulsePen in terms of central SBP and radial AI measurements ($P \leq 0.002$). However, in Bland–Altman analysis the difference in radial AI significantly increased proportionally to the mean value ($P < 0.001$). In summary, A_PULSE showed a good correlation of central hemodynamics with SphygmoCor and PulsePen, but with significant absolute differences.

Keywords: Tonometry; Augmentation index; Central blood pressure; A_PULSE

PO-261

TWO OFFICE BLOOD PRESSURE READINGS TAKEN ON EACH OF TWO VISITS ARE NOT ENOUGH FOR AN ACCURATE ESTIMATION AND AN ADEQUATE HYPERTENSION DIAGNOSIS

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Accuracy of Office Blood Pressure (OBP) estimation depends on the number of visits and the number of readings per visit. The goal of this study was to evaluate the accuracy of OBP estimations as a function of these two factors to check if two visits and two readings per visit provide sufficient accuracy.

A total of 828 series of OBP readings from 138 individuals (mean age 60.0, 82 with antihypertensive treatment, 60 women) were analyzed. Each individual made six visits separated at least 6 days and 13 BP readings were made on each visit at 2 minutes intervals with an automatic oscillometric validated device.

Duration of white coat effect was analyzed and readings previous to BP stabilization were removed. Confidence Intervals (CI) of 95% for mean BP values were calculated for each individual and each combination of number of visits and readings per visit. CI lengths were used to estimate accuracy. For Systolic BP (SBP), a CI length under 20 mm Hg was considered adequate, taking into account that most BP classification categories are defined based on 20 mm Hg increases of SBP.

Median difference between SBP average of the first three readings and the average of readings 4th, 5th and 6th was 3.1 mm Hg, with a 95% CI of (2.2, 4.2) mm Hg. The first three readings were removed for individual BP estimation. Percentiles of 90% were calculated for the CI length of SBP estimation in the non-treated subgroup.

Only for six visits and six or more readings per visit at least the 90% of the individuals achieved an adequate accuracy. Similar results were found for diastolic BP and treated individuals.

Currently followed guidelines to estimate OBP recommend two or more BP readings taken on two or more office visits. The results of this study suggest that two visits and two readings are not sufficient. In fact, good estimations for the majority of the individuals were achieved for six visits and six or more readings per visit (removing the first three).

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Table I. Ninety percent percentile of confidence interval length for SBP mean (mm Hg)

	4 readings	6 readings	8 readings
3 visits	61.3	45.0	43.4
5 visits	28.4	20.6	20.5
6 visits	21.8	17.1	17.5
Non-treated individuals			

Keywords: Office blood pressure; Number of blood pressure readings; Automatic blood pressure devices; White coat effect

PO-262

PREVALENCE OF SELF-MONITORING BLOOD PRESSURE AMONG ADULTS – HEALTHSTYLES, 2005 AND 2008

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Hypertension control remains below 50% in the United States. To increase control, JNC 7 recommends all hypertensive patients become active in their care through self monitoring of blood pressure (BP). We analyzed HealthStyles 2005 and 2008 survey to assess use of free BP checks and use of home BP devices to monitor blood pressure among adults; all estimates were based on self-reported data. The relative percent change (RPC) in the prevalence of these behaviors between 2005 and 2008 was assessed. There were a total of 10,218 adults aged 18 years and older in this report. Of these, 67.4% were normotensive and 32.6% were hypertensive. The proportion of hypertensive adults using free checks or home BP devices were 67.5% and 46.6%, respectively. Over the 3-year period, there were increases in the prevalence of monitoring BP by using free BP checks (RPC = 6.9%, 55.8% in 2008 vs 52.2% in 2005, $P < 0.05$) and home BP devices (RPC = 18.8%, 24.6% in 2008 vs 20.7% in 2005, $P < 0.05$). There were increases in proportion of hypertensive adults who reported using free checks (RPC = 1.6%, 68.0% in 2008 vs 66.9% in 2005, $P < 0.05$) and home BP devices (RPC = 14.1%, 49.4% in 2008 vs 43.3% in 2005). In 2008, hypertensive adults were 2.1 and 5.7 times more likely to use free BP checks and home BP devices, respectively. Based on 2005 and 2008 HealthStyles surveys, less than half of hypertensive adults used home BP device but more than half used free BP checks. Research to assess the impact of self-monitoring on patient medication compliance is warranted, especially in high risk groups. Health professionals should take advantage of the current interest in home BP monitors and free checks to improve patient motivation and compliance.

Keywords: Home blood pressure device; Hypertension; Free checks; Epidemiology

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PROGNOSTIC VALUE OF CLINIC AND AMBULATORY BLOOD PRESSURE MEASUREMENTS IN RESISTANT HYPERTENSION

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Progression to target organ damage and cardiovascular (CVD) risk are more closely associated with ambulatory (ABPM) than with clinic blood pressure (BP). Independent prospective studies have also found that the sleep-time BP mean is a better predictor of CVD risk than the awake or 24 hour BP means. Subjects with resistant hypertension are at a greater CVD risk than subjects with controlled BP with <3 BP-lowering medications. Moreover, non-dipping and nocturnal hypertension are highly prevalent in resistant hypertension. We compared to prognostic value of clinic and ambulatory BP in subjects with resistant hypertension participating in the MAPEC study, designed to test if bedtime chronotherapy with ≥1 hypertension medications exerts better BP control and CVD risk reduction than conventional therapy, i.e. all medications ingested in the morning. A total of 776 subjects with resistant hypertension, 387 men/389 women, 61.6 ± 11.2 years of age, were randomized to ingest all their prescribed hypertension medications upon awakening or ≥1 of them at bedtime. BP was measured by ABPM for 48 hour at baseline and again annually and more frequently (quarterly) if treatment adjustment was required. The median follow-up was 5.4 years (range 0.5–8.5 years). Based on the baseline ABPM profiles, the sleep-time mean of systolic BP was the best predictor of CVD risk in a Cox proportional-hazard model adjusted for sex, age, diabetes, and time of hypertension treatment (relative risk 1.31 [1.24–1.37], $P < 0.001$, for each 10 mm Hg increase in sleep-time BP). The corresponding risk associated with progressively increased clinic systolic BP was 1.16 [1.10–1.23]. Values associated with diastolic BP were much lower, and significant only for sleep-time mean. CVD risk was again more strongly associated with sleep-time BP on the basis of the ABPM profile closer to the events. ABPM is markedly superior to clinic BP in predicting CVD risk, rendering this technique as a requirement for proper CVD risk assessment in resistant hypertension. After adjustment for relevant contributing risk factors, only sleep-time systolic BP provides a significant prediction of outcome in a survival model that jointly included multiple clinic and ambulatory BP parameters.

Keywords: Cardiovascular risk; Resistant hypertension; Ambulatory blood pressure; Sleep-time blood pressure

PO-264

CAN PERSONAL EXPOSURES TO HIGHER NIGHTTIME AND EARLY MORNING TEMPERATURES INCREASE BLOOD PRESSURE?

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Environmental temperatures are inversely related to blood pressure. However, the effects of short-term temperature changes within a 24-hour period and measured with high accuracy at the personal-level have not been described. Fifty-one nonsmoking subjects living in the Detroit-area had up to five consecutive days of 24-hour personal-level environmental temperature (PET) monitoring along with daily cardiovascular measurements, including blood pressure (BP), performed mostly between 5 and 7 PM during summer and/or winter periods. The associations between hour-long mean PET levels over the previous 24 hours with the outcomes were assessed by linear mixed-models. Accounting for demographics, environmental factors, and monitoring compliance, systolic and diastolic BP were positively associated with several hour-long PET measurements ending from 10 to 15 hours beforehand. During this time, corresponding mostly to a period starting from between 1 and 3 AM and ending between 7 and 9 AM, an increase of 1°C was associated with a 0.81–1.44 mm Hg and 0.59–0.83 mm Hg elevation in systolic and diastolic BP, respectively. Modestly warmer commonly encountered PET levels posed a clinically-meaningful effect (e.g. a 6.95 mm Hg systolic pressure increase per inter-quartile range (4.8°C) elevation at lag hour 10). Community-level outdoor ambient temperatures were not related to BP. We provide the first evidence that personal exposure to warmer nighttime and early morning environmental temperatures might lead to an increase in BP during the ensuing day.

Keywords: Environmental conditions; Temperature; Climate; Blood pressure

PO-265

TWENTY FOUR-HOUR AMBULATORY BLOOD PRESSURE (ABP) AND CARDIOVASCULAR EVENTS IN ELDERLY HYPERTENSIVE PATIENTS FOLLOWED-UP FOR 7 YEARS

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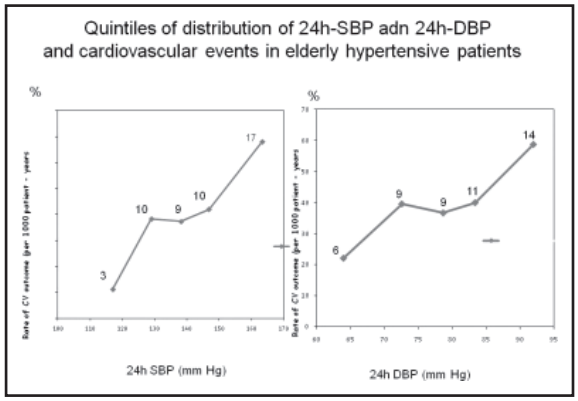
Introduction: It is still uncertain whether 24-hour ambulatory blood pressure (ABP) predicts cardiovascular (CV) events in elderly hypertensive patients.

Methods: After ABP, we followed-up for 7.0 years, range 0.2–14.4) a population of 179 elderly hypertensive patients (>65, mean 70.0 ± 4.5 years, 95 women. BMI 27.2 ± 4.3 kg/m^2), under stabilized antihypertensive medication and without previous CV events,

Results: Occurrence of first CV events was followed for 1258 patients-years. There were 49 first CV fatal/non-fatal events (27 strokes, 10 coronary, 12 other cardiovascular events). At baseline, patients who subsequently had an event were significantly older 71.5 ± 4.9 vs 69.4 ± 4.2 years ($P < 0.001$), had higher values of 24 hour SBP 145 ± 17 vs 136 ± 16 ($P < 0.01$), of nighttime SBP 136 ± 20 vs 126 ± 19 mm Hg ($P < 0.001$) and of 24 hour and nightime Pulse Pressure (PP) respectively 65.8 ± 16.7 vs 59.3 ± 12.5 ($P < 0.05$) and 65.2 ± 17 vs 58.2 ± 13 ($P < 0.02$). No significant differences were found for metabolic parameters and casual BP. In a Cox regression analysis SBP and PP (24 hour and nighttime) values as well as 24 hour SBP variability (SD) were independent ($P < 0.05$) predictors of subsequent total CV events after adjustment to age, BMI, diabetes, medication, and casual SBP. Concerning stroke, when the sample was divided by the cut off of PP< vs ≥55 mm Hg significant survival curves free of stroke were observed (log rank 5.58 $P < 0.02$). Figure 1 shows the rate of CV outcome per 1000 patient – years for the quintiles of distribution of baseline 24 hour-SBP and 24 hour-DBP for CV events (Figure 1). As shown no J shape curve was observed in the relation events vs 24 hour-systolic and diastolic

BP. Conclusions. In elderly patients ABP especially high 24-hour SBP and 24-PP and 24 hour SBP variability are strong predictors of cardiovascular events.



Keywords: Ambulatory blood pressure; Prognosis; Elderly

PO-266

TOTAL PERIPHERAL RESISTANCE AND ITS RELATIONSHIP WITH HYPERTENSION IN PATIENTS WITH SEVERE SLEEP APNEA

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Introduction: The sleep apnea syndrome (SAS), in a possible factor which is behind many hypertensive situations which are sometimes difficult to treat. However, despite it is a frequent situation, there are few data about possible mechanisms that cause hypertension in these patients (P).

Objective: To study some factors that may explain the presence of hypertension in P with SAS.

Material and Methods: We studied, 12 P diagnosed by polysomnography of SAS and they were compared with another group of 20 normal persons. In all of them we measured systolic and diastolic central blood pressure (SCBP, DCBP), central pulse pressure (CPP), total peripheral resistance (TPR) and systolic/diastolic peripheral blood pressure (S/D PBP)

Results: Data were compared and showed in the following Table.

Conclusions: It is evident that P with SAS, had not only significantly more central blood pressure than normal persons but also higher CPP and TPR indicating the high vascular risk of these P showing also, that this last factor (TPR) could be behind the higher levels of blood pressure that they present.

Table Comparative table of SAS and normal

Data	SCBP	DCBP	CPP	TPR	S/D PBP
SAS	129 ± 3*	86 ± 4*	45 ± 3*	1.5 ± 0.2*	152/96 ± 9/6*
Normal	98 ± 2	78 ± 3	26 ± 4	1 ± 0.1	124/81 ± 3/4

*Means P value <0.05

Keywords: Peripheral resistance; Hypertension; Sleep apnea; Central pressure

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PATIENTS WITH HYPERTENSIVE CRISIS HAVE HIGHER RISK FOLLOWING FIRST MONTH AFTER THE CRISIS COMPARED WITH HYPERTENSIVE PATIENTS AT SIMILAR BLOOD PRESSURE

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Causes of hypertensive crisis (HC) are well known, however, the impact of the sudden pressure elevation on arterial wall are less known.

Objective: To evaluate arterial stiffness and peripheral resistance of patients (P) with HC compared with hypertensive P without HC (PHTA) at first month after the HC, with similar brachial blood pressure level.

Material and Methods: We studied 22 P with HC (52 ± 8 years old) after the first month of the HC and compared with 68 PHTA (59 ± 7 years old) with similar blood pressure (<140/90 mm Hg). In all of them we measured augmentation index (AI), total peripheral resistance (TPR), 24 hours microalbuminuria (MICRO). Results were compared and showed below:

Conclusions: Those P with HC have high risk after the first month of the HC principally considering the increased value of AI and MICRO they have, compared with PHTA at similar brachial blood pressure level. We should follow these P till to achieve normalize their situation again.

Table I. Comparative table of patients with HTA and HC

Data	AI	TPR	MICRO
HC	36 ± 5*	1.7 ± 0.5*	39 ± 9*
PHTA	21 ± 3	1.1 ± 0.1	18 ± 7

*Means P value <0.05

Keywords: Hypertensive crisis; Arterial stiffness; Peripheral resistance

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CORRELATION BETWEEN LEFT VENTRICULAR MASS (LVM) AND AMBULATORY OR CLINIC BLOOD PRESSURE (BP) IN VERY ELDERLY SUBJECTS

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LVM is positively related to BP and the relationship is closer for ambulatory (A) as compared to clinic (C) values. Limited information exists as to whether this is the case also at a very advanced age. We studied 82 patients (71 males and 11 females) older than 90 years (age 94 ± 3.6 years, mean ± SD). LVM was assessed by echocardiography and indicized (I) to either body surface area (BSA) or height at -2.7. BP was measured both in the clinic environment (via standard methodology) and automatically over the 24 hours. Clinic BP was 121.42 ± 17.03/70.07.2 ± 9.49 (systolic/diastolic) mm Hg; 24 hour mean BP was 129.0 ± 16.17/65.24 ± 8.56 mm Hg, with only little difference between day and night values; LVMI/BSA was 121.6 ± 40.8 g/m^2 and LVMI/

height-2.7 54.5 ± 18.9 there was a significant ($P < 0.001$) correlation between LVMI values and both clinic or ambulatory systolic BP regardless how LVMI was calculated. The correlation coefficients were somewhat lower than those reported for younger populations. Like in younger population a somewhat closer relationship was seen between LVMI and ambulatory vs clinic BP and for systolic vs diastolic BP. LVMI showed a much weaker correlation with clinic and ambulatory diastolic BP. Systolic BP correlated also with left atrial dimension ($P < 0.001$) again somewhat more closely when ambulatory rather than clinic BP was considered.
In conclusion, even in very elderly subjects LVMI is related to and possibly depends on BP levels. Like in younger individuals BP load over the 24 hours appears to be a somewhat better determinant of alterations in cardiac structure than BP measured in the doctor's office.

Keywords: Left ventricular mass; Ambulatory blood pressure; Clinic blood pressure; Very elderly subjects

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CLINICAL AND AMBULATORY BLOOD PRESSURE (BP) VALUES IN CENTENARIES

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The difference between clinic and ambulatory BP increases with age. Data, however, are mainly available in subjects aged up to 80–85 years and limited information exists on older ages. We studied 11 patients, all females, aged 100 years or more (101.5 years, range 100–104), hospitalized in our Geriatric Institute. Seven patients had a history of hypertension but none was under antihypertensive treatment. Mild cognitive impairment was diagnosed in 10 patients. Five patients had a history of myocardial infarction but none of stroke. Clinic BP was the mean of two measurements performed in the sitting position after 5 minutes of rest. Ambulatory BP was recorded for 24 hours with automatic readings spaced by 20 minute intervals. The recordings were carried out successfully in all circumstances and no subject reported problems with night sleep.
Clinic BP was 111.8 ± 12.5/68.2_8.73 mm Hg (systolic/diastolic, mean ± SD). Mean 24 hour BP was 122.44 ± 13.31/63.22 ± 5.47 mm Hg, The day and night BP values were 123.3 ± 11.94/64.8 ± 5.47, 121.77 ± 15.44/59.77 ± 5.71 mm Hg, respectively.
In conclusion, the progressively greater difference between clinic and ambulatory BP associated with aging reverses above a certain age because in centenaries no difference between clinic and ambulatory BP is apparent. Confirming previous reports centenaries appear to loose the day-night BP circadian rhythm.

Keywords: Centenaries; Ambulatory blood pressure; Clinical blood pressure; Hypertension

PO-270

USEFULNESS OF AUTOMATED OFFICE BLOOD PRESSURE MEASUREMENT BY BPTRU FOR THE DIAGNOSIS OF RESISTANT HYPERTENSION

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Resistant hypertension (unmet blood pressure goal despite full doses of three or more drugs, including a diuretic) is a relevant clinical problem for primary care clinicians and specialists. Clinical trials and large population surveys suggest that it is not rare, involving perhaps 20–30%. The diagnosis of resistant hypertension requires use of precise blood pressure techniques since, in this setting, it is crucial to exclude pseudoresistance due to white-coat phenomenon.
In this study we compare three different techniques of blood pressure (BP) measurement – office BP (OBP), automated office BP (AOBP) and ambulatory BP (ABP) – for the diagnosis of resistant hypertension.
Sixty-five consecutive hypertensive patients presenting with OBP (average of three sphygmomanometric readings obtained in standardized conditions) >140/90, despite three or more antihypertensive drugs, including a full diuretic dose, were considered.
During a second visit (in which resistant status was confirmed) all patients underwent AOBP measurement using the BpTRU device (VSM M.T.Ltd, Canada). BpTRU is an automated oscillometric monitor, designed to take a first reading while the physician is present, and then to average five measurements while the patients is alone in the consulting room.
Data obtained with OBP and AOBP were compared with daytime mean ABP values, obtained by a validated device.
Comparison of office blood pressure (OBP), automated office blood pressure obtained by BpTRU (AOBP) and daytime ambulatory blood pressure (ABP) in 65 hypertensive patients.
As expected, OBP measurement, even performed in standardized fashion, overestimated patients' BP values ($P < 0.025$ v. AOBP and ABP). Furthermore, using daytime ABP mean values as reference, OBP misclassified 14 subjects (21.5%). On the contrary, AOBP identified all but one of the resistant hypertensive subjects and no significant difference between AOBP and ABP mean values was found.
In conclusion, also in the particular setting of resistant hypertension, in which exact BP values are extremely important for the diagnosis, prognosis and treatment decisions, the BpTRU monitor, provided reliable information on the true BP status of the patients.

	OBP	AOBP	ABP
Systolic BP mm Hg ± SD	169 ± 19	156 ± 20	155 ± 19
Diastolic BP mm Hg ± SD	92 ± 11	86 ± 10	85 ± 10

Keywords: Resistant hypertension; Automated office blood pressure; Ambulatory blood pressure

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EFFECTS OF ALISKIREN- AND RAMIPRIL-BASED TREATMENT ON CENTRAL AORTIC BLOOD PRESSURE IN SYSTOLIC HYPERTENSION

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Background: Central aortic blood pressure (BP) is a stronger predictor of cardiovascular mortality and morbidity than brachial BP. The AGELESS (Aliskiren for GEriatric LowEring of SyStolic hypertension) study showed that in patients aged ≥65 years with systolic hypertension, a direct renin inhibitor (aliskiren)-based regimen was more efficacious in lowering peripheral BP than an ACE-inhibitor (ramipril)-based regimen.

Objective: In a subgroup of the AGELESS study, we studied the effect of both regimens on central aortic BP.

Methods: In this 36-week double-blind study, 901 elderly patients with systolic hypertension were randomized to aliskiren (150–300 mg; n = 457) or ramipril (5–10 mg; n = 444); hydrochlorothiazide (12.5–25 mg) was added from week 12 and amlodipine (5–10 mg) from week 22 if mean sitting systolic blood pressure (SBP) ≥140 mm Hg. Central aortic BP was assessed from the radial artery waveform using a transfer function with the Sphygmocor device in a subgroup of 125 patients at baseline and after 36 weeks of treatment.

Results: The aliskiren regimen provided numerically larger reductions than the ramipril regimen in both mean sitting peripheral SBP (between-treatment difference for aliskiren vs ramipril, -1.9 mm Hg [95% CI -4.0, 0.2]; $P = 0.075$) and mean central aortic SBP (between-treatment difference for aliskiren vs ramipril, -3.1 mm Hg [95% CI -7.1, 0.9]; $P = 0.123$).

Conclusions: Aliskiren-based therapy provided numerically greater reductions in central aortic BP than a ramipril-based regimen in elderly patients with systolic hypertension. Table 1 summarizes the results.

Table 1.

	Aliskiren-based regimen	Ramipril-based regimen
Overall population	n = 451*	n = 439*
Baseline peripheral SBP (mm Hg)	156.5 ± 10.9	156.6 ± 10.6
Change in peripheral SBP from baseline to week 36	-20.0 ± 0.8	-18.1 ± 0.8
Central Aortic SBP Population (substudy)	n = 59*	n = 66*
Baseline (mm Hg)	125.7 ± 11.1	129.8 ± 9.4
Week 36 endpoint (mm Hg)	108.9 ± 12.0	113.5 ± 10.9
Change in central aortic SBP form baseline to week 36 (mm Hg)	-17.5 ± 1.8	-14.4 ± 1.8

*Number of patients with data at baseline and week 36 endpoint.

Keywords: Central aortic blood pressure; Systolic hypertension; Elderly; Aliskiren

PO-272

APPARENT TREATMENT RESISTANT HYPERTENSION IN A COMMUNITY-BASED PRACTICE NETWORK

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Treatment resistant hypertension (TRH), defined as a blood pressure (BP) above goal on ≥3 or at goal on ≥4 medications, occurs in 20–30% of patients in clinical trials, but the prevalence in community-based practices (CBP) is not known. The Outpatient Quality Improvement Network (O'QUIN) Hypertension Initiative clinical database, obtained from 197 outpatient practices in the Southeast was examined for January 2008 through June 2010. A total of 387,013 unique treated hypertensive patients were identified. Data (mean [SD], %) are summarized in the Table. Since medication adherence and BP measurement artifacts are not available in this database, the term apparent (a) TRH is used (Figure 1). BP was controlled to goal in 65% of patients without and 40% of patients with diabetes (DM) and/or chronic kidney disease (CKD) in O'QUIN. Patients with DM and CKD received more medications and achieved lower BP even though they were less likely to be controlled to the more stringent goal of <130/<80. African Americans were comparatively over-represented among the groups with diabetes and/or CKD and in the uncontrolled groups. Overall, 25.2% of treated hypertensive patients met the definition of aTRH with BP uncontrolled on ≥3 medications (17.7%) and controlled on ≥4 medications (7.5%). The high proportion of under-treated uncontrolled patients (1–2 medications) suggests therapeutic inertia remains an obstacle to better BP control. Practical clinical trials are needed to address both the challenge of therapeutic inertia and the substantial burden of TRH in CBP in order to reduce racial disparities and realize more of the evidence-based benefits of BP control.

Table.

	BP <140/<90 No DM, CKD	BP ≥140/≥90 No DM, CKD	BP <130/<80 DM &/or CKD	BP ≥130/≥80 DM &/or CKD
Number, %	153,489, 65%	84,010, 35%	59,408, 40%	90106, 60%
Age, M±SD	61.4±15.5	60.8±15.5	66.2±13.7	63.9±13.8
Race, C:AA	2.1 : 1	1.5 : 1	1.5 : 1	1.1 : 1
Wt, kg, M±SD	87.8±22.0	90.6±24.5	94.0±23.7	97.4±24.1
SBP, M±SD	121.8±11.2	150.5±14.8	115.6±10.0	142.6±16.1
DBP,M±SD	73.1±9.1	86.5±11.6	66.4±8.1	80.1±16.1
BP meds, M±SD	2.1±1.1	2.2±1.2	2.6±1.3	2.6±1.3
1 BP Meds, %	41%	38%	26%	26%
2 BP meds, %	31%	31%	28%	27%
3 BP Meds, %	18%	19%	23%	24%
4+ BP Meds,%	10%	12%	23%	23%

Keywords: Treatment resistant; Hypertension; Community-based network

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PROGRESSION FROM PRE-HYPERTENSION TO HYPERTENSION IS ACCELERATED IN AFRICAN AMERICANS

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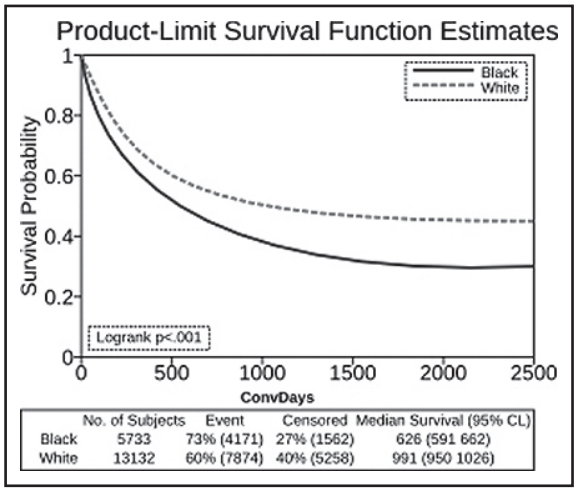
The clinical trajectory of pre-hypertension to hypertension is influenced by multiple clinical and demographical factors. This study examined differences in conversion rates between blacks and whites in a prospective cohort study of 18,865 persons (5733 [30.4% black, 13,132 [69.6%]) white) ≥18 years old. Data come from a consortium of outpatient clinics participating in the Outpatient Quality Improvement (O'QUIN) Hypertension Initiative. Observation was censored at the 2550th day. Days elapsing from the date of entry in the study to date of conversion to hypertension (systolic blood pressure [SBP] ≥140 and/or diastolic [D]BP ≥90 mm Hg) established the conversion time



(T). Data analysis relied on Cox regression modeling to examine the risk of conversion as a function of racial differences controlling for baseline SBP, DBP, body mass index [BMI], chronic kidney disease [CKD], diabetes, age, and gender. Our finding demonstrated significant disparities between blacks and whites. The median conversion time [S(T)50] of blacks was 365 days earlier than whites after controlling for covariates (Figure 1). The strongest predictor of conversion was baseline SBP. Hazard Ratio (HR) of persons with Stage 2 pre-hypertension, i.e. baseline SBP 130–139 mm Hg, was the highest (HR = 1.77, 95% CI: 1.69–1.86), followed by "Stage 1" pre-hypertension (SBP 120–129) in reference to normotensives, i.e. SBP $\leq$ 119. Risk of conversion increased with advancing age and BMI (both $P < 0.001$). Baseline diastolic BP has also strong effect on conversion albeit at a lesser strength than SBP. Diabetes was a significant risk factor for conversion (HR = 1.13, 95% CI = 1.08, 1.19) while CKD retained borderline significance (HR = 1.16, 95% CI = 1.00, 1.359). These findings raise the possibility that interventions, including pharmacological options, in pre-hypertension could be useful for reducing the racial disparities in the prevalence of hypertension and its downstream complications (Figure 1).

Keywords: Pre-hypertension; Hypertension; Racial disparities

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CLINICAL CHARACTERISTICS OF PATIENTS WITH UNCONTROLLED AND APPARENT TREATMENT RESISTANT HYPERTENSION: NHANES 2005–2008

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Background: While hypertension control to <140/<90 mm Hg improved to 50% (NHANES 2007–2008), millions of patients remain uncontrolled. Defining characteristics of uncontrolled hypertensive patients may facilitate efforts to improve blood pressure (BP) control.

Methods: Subjects included 13,375 hypertensive adults from National Health and Nutrition Examination Surveys (NHANES) 1988–2008 subdivided into 1988–1994, 1999–2004, 2005–2008. Uncontrolled hypertension was defined as BP <140/<90 mm Hg and apparent treatment resistant (aTRH) if the patient reported taking $\geq$3 antihypertensive medications. Framingham 10-year coronary risk (FCR) was calculated. Multivariate regression was used to identify independent predictors of untreated, treated uncontrolled, and aTRH.

Results: The majority of uncontrolled hypertensives were untreated across surveys. Multivariate predictors of untreated hypertension in all three NHANES survey periods, i.e. consistent, included male sex (odds ratio 2.26–2.73 95% confidence intervals [1.86–3.51]), infrequent (0–1) healthcare visits/year (4.66–4.95 [3.11–6.94]), body mass index <25 kg/m^2 and <Stage 3 chronic kidney disease ([CKD], 1.67–2.28 [1.10–3.66] and FCR <10% (7.65–8.61 [4.78–12.26]). Most treated, uncontrolled patients reported taking 1–2 BP medications. Predictors of treated, uncontrolled hypertension across surveys included increasing age (1.19–1.30 [1.06–1.42]/10 years), black race/ethnicity (1.43–1.47 [1.13–1.85]), and FCR >20% (1.81–2.93 [1.27–3.86]). The percentage of uncontrolled hypertensives with aTRH increased over time (15.9% vs 28.0%, $P < 0.01$). Predictors of aTRH included obesity (2.04 [1.17–3.53], CKD (2.52 [1.75–3.62]) and FCR >20% (4.29 [1.95–9.42]) with age and black race/ethnicity significant in 2005–2008.

Conclusions: Strategies to increase healthcare use by people that are disproportionately male, lean and low 10-year FCR could improve hypertension treatment and control. Targeted strategies are needed to offset projected increases in uncontrolled treated and aTRH given population health trends to older age, more ethnic minorities, and a higher prevalence of obesity complicated by CKD and other coronary risk equivalents.

Keywords: Clinical characteristics; Uncontrolled; Treatment resistant; Hypertension

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IMPACTING POPULATION CARDIOVASCULAR HEALTH THROUGH A COMMUNITY-BASED PRACTICE NETWORK: UPDATE ON AN-ASH-SUPPORTIVE COLLABORATIVE

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The Hypertension Initiative began in 1999 to facilitate the transition of South Carolina from a leader in cardiovascular disease (CVD) to a model of heart and vascular health. The goals were to reduce heart disease and stroke by 50% by promoting healthy lifestyles and access to effective care and medications. Practice data audit with provider feedback reports was the key tactic for improving hypertension, hyperlipidemia and diabetes management.

The Experts in Hypertension Seminar Series began in 1999 and serves three purposes. (1) continuing medical education (CME) on evidence-based approaches to CVD risk factor management, (2) recruiting community-based providers and practices into a network with audit and feedback and (3) encouraging physicians to become American Society of Hypertension (ASH) certified Clinical Hypertension Specialists and champion community CVD risk factor control. With ASH support, the network grew to 197 practices with ~2,000,000 patients in six states. Summary data are collected from various electronic health record systems (EHRS) and quarterly feedback reports are generated. From 2000 to 2005, BP control in 208,547 hypertensives improved from 49% in 2000 to 66% in 2005. Of 82,442 diabetic, dyslipidemic hypertensives HbA1c control to <7% improved from 49% to 54%, LDL-cholesterol control to <100 mg/dL rose from 38% to 57%, and BP control to <130/<80 advanced from 22% to 35%. S.C. improved from 51st to 35th in cardiovascular mortality from 1995 to 2006, the largest improvement in Southeastern States. The Hypertension Initiative has expanded to the Outpatient Quality Improvement Network (O'QUIN) to include comparative effectiveness research and other chronic diseases. Lessons learned include: (1) trust enables success, (2) addressing needs and priorities or practices engenders their active participation, (3) infrastructure support must be multilateral (4) ongoing strategic planning is essential to uncover opportunities and avoid pitfalls. Future progress may be accelerated through a better organized network and strategic planning, which includes (1) strengthening CME needs assessment and documenting changes in evidence-based practice (2) building a robust comparative effectiveness research program (3) facilitating meaningful use of EHRS and pay-for-performance incentives. The goal is a network that can produce positive and sustainable impacts on CVD and other chronic diseases that can be amplified over time.

Keywords: Cardiovascular health; Community-based-practice network

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ESTIMATION OF CENTRAL CARDIOVASCULAR PARAMETERS FROM BRACHIAL CUFF PRESSURE WAVEFORM

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Measurement of central cardiovascular parameters is important to evaluate arterial stiffness and other cardiovascular risk. Previously, applanation tonometry is widely used to estimate central cardiovascular parameters such as augmentation index (AI), and traveling time of reflection (Tr). However, in this method, it is recognized that measurement accuracy highly depend on operators' skill, and the measurement is time consuming. To overcome these limitations, we newly designed a device to estimate the central cardiovascular parameters from the measurement of brachial cuff pressure wave. In our method, two separate air bags are integrated into a single brachial cuff unit to measure the pulse wave with the peripheral artery occluded by supra-systolic pressure. Furthermore, peripheral to central transfer functions are individualized based on patients' age, height, and brachial SBP. The purpose of this study is to validate the accuracy of this new device by comparing two parameters, AI and Tr, derived from brachial cuff pressure waveforms and from carotid tonometry waveforms. Measurement was repeated twice for 200 subjects at rest, aged 23–88 year, brachial blood pressure was $124 \pm 17/75 \pm 12$ mm Hg (systolic/diastolic). We found that AI and Tr derived from brachial pressure waveforms were closely related with those of carotid tonometry waveforms: $r = 0.86$ for AI and $r = 0.89$ for Tr. Reproducibility of the device was higher than that of carotid tonometry: SD of Tr was 4.3/13 ms, SD of AI was 6.0/7.0% (brachial/carotid). In conclusion, the results indicate that AI and Tr can be estimated reliably using pressure waveforms measured by the cuff at the brachial artery.

Keywords: Central pressure waveform; Brachial cuff pressure; Augmentation index; Time of reflection

PO-277

BLOOD PRESSURE MEASUREMENT-DEVICE AND CALIBRATION PATTERNS IN HOME HEALTH CARE

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Home health care visits number over 100,000,000 visits serving over 3,000,000 patients in 2006. The measurement of blood pressure is one of the standard vital signs in patients that is often a critical aspect of their disease management. Device usage (type and cuff options) and calibration schedules are often not subject to evaluation. Much has been published regarding the improper measurement of BP, in part related to device selection and proper cuff size-thereby resulting in inaccurate BP. We developed a simple survey to ascertain to device usage, cuff options, and calibration schedules that might result in improper BP measurement beyond that of the observer technique. We telephoned 60 agencies. Not all agreed to respond-thus the results are based upon responders only. Our findings suggest multiple areas of concern that require additional surveying. The vast majority of devices being used are of the manual aneroid type. These fairly fragile devices are subject to rapid deterioration and loss of calibration upon exposure to changes in temperature (both the hot and cold) mild trauma and extended use. The conditions that may exist in the home care environment may result in a more rapid loss of calibration then when placed in the home itself. The absence of a fixed calibration schedule of devices in almost 96% of agencies is an area of concern. Although a significant percentage of agencies provide additional cuff sizes the majority still do not. Also we have no information to determine if proper sized cuffs are being used. The determination if distributed devices are both calibrated and being used properly is beyond the scope of this abstract. The usage of aneroid devices, the predominance of the distribution of a single cuff and the lack of a calibration schedule all represent potential sources of improper BP measurement in the home care environment (over and above the other issues of BP measurement detailed by others).

Table I. BP Device Responders

Agency number	Nurse number	Agency supplies device %	Manual device %	Automated devices	Additional cuffs (%)	Calibration fixed
21	751	518 (60.8%)	8834 (98%)	17 (2%)	358 (42%)	35 (4.1%)

Keywords: Home health care; Blood pressure device calibration; Cuff; Aneroid or automatic

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ABPM IN OCTOGENARIANS

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Life expectancy in Israel is increasing. 2.7% of Israel's population is aged 80+. Hypertension is very common in this population. In recent years, 24-hours ambulatory blood pressure monitoring (ABPM) became a valuable tool to evaluate hypertension. Yet, relatively few works concentrated on ABPM in octogenarians.

Between 11/2008 and 9/2010, 286 ABPMs in octogenarians were performed in our service. Of which 200 had at least 34 successful measurements and at least one measurement for each hour of sleep. The demographic and clinical data of these 200 were collected and analyzed. Measurements taken during day sleep ("Siesta") were included in the sleep hours.

The average age was 84 ± 3 years, 43% were men. The average BMI was 26 ± 3.

There were 53 ± 7 measurements per test, 37 ± 8 during day time and 16 ± 4 during sleep time. The average sleep duration was 8 ± 2 hours.

Primary care physicians ordered 70% of tests, hypertension specialists 20% and other physicians 10%. The reason for ordering the test was "evaluation of BP" In 74.5%, recurrent falls in 10%, labile hypertension in 7.5%, masked hypertension in 5% and white coat hypertension in 3%.

Masked hypertension was diagnosed in 25% of the cases, white coat hypertension in 13%.

Seventy-two percent were non dippers, of which 60% demonstrated reverse dipping. There was no correlation between subjective sleep disorders and dipping pattern.

Sixty-two percent had dyslipidemia, 29% Diabetes, 29% IHD, 25% CKD, 20% depression, 19% stroke and 11% heart failure. Eighty-eight percent were taking anti hypertensive treatment, 68% statins and 48% aspirin. The average number of antihypertensive medications per patient was 2.65. Cardio vascular and renal morbidity were significantly higher in subjects with a 24 hour average of $\leq$130/80 ABPM compared with $\leq$140/80.

Diabetics had a significantly higher incidence of CKD and IHD. The average clinic BP was significantly higher – 152/74 vs142/71 in non – diabetics. Seventy-eight percent of the diabetics were non-dippers as compared to 69% of non-diabetics.
ABPM is possible and reasonable in the very elderly. The main findings in this age group were high rate of masked hypertension and non-dipping. Further studies are needed to define the "normal" vakues for this age group.

Average ± SD				
	SBP	DBP	Heart Rate	SBP Variability
Clinic	145 ± 23	73 ± 12	67 ± 13	
24 hours	137 ± 15	67 ± 7	62 ± 9	18 ± 9
Awake	139 ± 15	69 ± 7	64 ± 10	16 ± 4.5
Sleep	134 ± 18	64 ± 12	59 ± 9	15 ± 10

Keywords: ABPM; Age; Octogenarians

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IMPACT OF INITIAL ANTIHYPERTENSIVE TREATMENT WITH A SINGLE-PILL COMBINATION ON BLOOD PRESSURE (BP) GOAL ATTAINMENT: A MATCHED COHORT STUDY

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Clinical trials suggest that the time-to-achievement of target BP is an important determinant of long term outcomes. This study evaluated the real-world impact on BP control rates of initiating antihypertensive treatment with a single-pill combination (SPC) vs initiating monotherapy and subsequently switching to a SPC (switcher) at the discretion of the treating physician. Electronic medical records from a large integrated health delivery system were analyzed for the period between 01/2005 and 11/2009. Adult patients with uncontrolled BP initiating SPC were matched 1:1 with switcher patients based on exact matching factors and propensity scores. Kaplan–Meier rates of BP control achievement and mean systolic and diastolic change over time were compared between matched cohorts. SPC and switcher cohorts (896 subjects in each group), were well-matched with respect to age (mean 58 years), gender (51% female), baseline BP (mean 153/88 mm Hg), BP stage (stage 2- 43%), concomitant medications, co-morbidities, and healthcare resource use at baseline. During treatment follow-up, the proportion of patients achieving BP control was consistently higher in the SPC than switcher group (3 months: 26.3% vs 16.6%; 6 months: 47.3% vs 40.2%; 12 months: 71.9% vs 70.4%), resulting in significantly shorter median time to achievement of goal BP for the SPC cohort (6.4 vs 7.2 months, Log-rank $P = 0.0396$). The impact of SPC on BP control was more pronounced among the subset of patients with stage 2 hypertension (3 months: 29.9% vs 16.9%; 6 months: 51.7% vs 37.9%; 12 months: 72.6% vs 66.1%; median time to BP control: 5.5 vs 7.9 months, $P = 0.0157$). After 3 months of therapy, the mean BP reduction was 19/10 mm Hg for the SPC group compared to 13/7 mm Hg for the switcher group. For patients with stage 2 hypertension, the mean BP reduction was 29/13 and 22/10 mm Hg for SPC and switchers, respectively. This real-world matched-cohort study showed that initiating treatment on SPC was associated with better and more rapid BP control, especially in patients with stage 2 hypertension, compared to patients initiating monotherapy and subsequently switching to SPC.

Keywords: Hypertension; Antihypertensive therapy; Single-pill combination; Blood pressure

PO-280

INFLUENCE OF DIPPING CLASSIFICATION ON FASTING GLUCOSE IN SUBJECTS WITH AND WITHOUT ELEVATED AMBULATORY BLOOD PRESSURE: THE HYGIA PROJECT

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Non-dipping has been identified as a significant marker of cardiovascular risk, independent of the blood pressure (BP) level. Independent prospective studies have also found that the sleep-time BP mean is a better predictor of cardiovascular risk than the awake or 24 hour BP means Moreover, elevated fasting glucose is also linearly correlated with increased cardiovascular morbidity and mortality. Accordingly, we evaluated and compared the relative influence of the sleep-time relative BP decline, sleep-time BP mean, and awake BP mean on fasting glucose in subjects participating in the Hygia Project, designed to evaluate prospectively cardiovascular risk by ambulatory BP monitoring (ABPM) in primary care centers of Northwest Spain. We studied 6120 subjects (3328 men/2792 women; 5370 hypertensive), 61.8 ± 13.5 years of age. Hypertension was defined as an awake BP mean ≥135/85 mm Hg for systolic/diastolic BP, or an asleep BP mean ≥120/70 mm Hg, or BP-lowering treatment. BP was measured by ABPM for 48 hour. Subjects were divided in four groups according to BP level (normal or high BP, using the thresholds provided above) and to sleep-time relative systolic BP decline (dipper or non-dipper). Glucose was significantly higher in non-dippers than in dippers both among those with normal BP (108.0 vs 105.1 mg/dL; $P = 0.011$) as well as in subjects with elevated ambulatory BP (111.8 vs 105.2 mg/dL; $P < 0.001$). Mean glucose was comparable between dipper subjects with normal and high BP ($P = 0.886$). When subjects were classified according to the level of awake and asleep BP means, glucose was significantly greater in subjects with high sleep-time BP mean, independently of the value of awake BP ($P < 0.001$). Plasma glucose is significantly elevated with a progressive loss in proper sleep-time BP regulation and the corresponding decrease in sleep-time relative BP decline, independently of awake BP mean. The awake and 24 hour mean BP values are not significantly correlated with glucose when results are corrected by sleep-time BP. These results suggest that an elevated asleep BP mean might have higher prognostic value than clinic or awake BP.

Keywords: Glucose; Dipping; Ambulatory blood pressure

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INFLUENCE OF DURATION OF AMBULATORY BLOOD PRESSURE MONITORING (48 VS 24 HOURS) ON CARDIOVASCULAR RISK ASSESSMENT

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Independent prospective studies have found that ambulatory blood pressure (BP) monitoring (ABPM) is more closely

correlated with target organ damage and cardiovascular disease (CVD) risk than clinic BP determination. All these studies have been based on a single baseline 24 hour ABPM profile, without accounting for changes over time in the level and pattern of BP and, most important, without taking into account that reproducibility of any estimated prognostic ABPM parameter depends markedly on duration of sampling and not on sampling rate. We evaluated the influence of the duration of ABPM and frequency of BP sampling on CVD risk assessment in the MAPEC study, where subjects were systematically evaluated by periodic ABPM. We evaluated 3344 subjects (2610 hypertensive, 1718 men/1626 women), 52.6 ± 14.5 years of age. BP was measured at 20-minutes intervals from 07:00 to 23:00 hour and at 30-minutes intervals at night for 48 hour at baseline and again annually or more frequently (quarterly) if treatment adjustment was required. The Cox proportional-hazard model was used to analyze CVD risk associated with increased mean BP values estimated from the original ABPM profiles, from the first 24 hour of ABPM at the original 20–30 minutes intervals, and from ABPM series obtained by keeping just one BP reading every 2 hour for 48 hour. The median follow-up was 5.6 years (range 0.5–8.6 years). Bland-Altman plots indicate that the awake, asleep and 24 hour BP means are better reproduced with data sampled every 2 hour for 48 hour (up to 24 BP values) than by data sampled at 20–30 minute intervals for just 1 day (up to 64 BP values). Relative CVD risk for those mean BP values, adjusted by significant confounding factors including age, sex and diabetes, was significantly overestimated by up to 48% for systolic BP and underestimated for diastolic BP using the first 24 hour of sampling. Relative CVD risk, however, differed by <2% for all ABPM characteristics estimated using data sampled at the lower rate of 2 hour for two consecutive days. This study on subjects evaluated prospectively by repeated 48 hour ABPM corroborates that reproducibility of mean BP values depends on duration of monitoring but not on sampling rate. CVD risk associated with increased ambulatory BP is very poorly estimated using the common 24 hour ABPM, clearly insufficient for a proper diagnosis of hypertension and for CVD risk stratification.

Keywords: Ambulatory blood pressure; Cardiovascular risk; Sampling requirements

PO-282

REPRODUCIBILITY OF NOCTURNAL BLOOD PRESSURE DIPPING IS INFLUENCED BY DAY-TO-DAY CHANGES IN SLEEP QUALITY

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A blunted nocturnal BP fall during ambulatory BP monitoring (ABPM) is associated with an increased risk of cardiovascular events. However, the reproducibility of nocturnal BP dipping and its relationship to variations in daytime physical activity and sleep quality are not well-established. We examined the reproducibility of the nighttime BP dip in 127 African American and White men and women who were not treated with antihypertensive medications and who had no history of diabetes, chronic kidney disease, or sleep apnea. ABPM data was acquired on 3 typical workdays separated by approximately 1 week. Sleep quality and daytime physical activity were assessed using a wristwatch-style actigraph. Sleep quality was quantified as the fragmentation index (derived from the frequency and duration of arousals); daytime activity was expressed as the average activity counts/min during the waking period.

The study cohort included 127 subjects with a mean age of 45.7 ± 8.6 years; 41% were female and 39% were African-American. The average awake ambulatory BP was 136.4 ± 10.5/83.8 ± 8.0 mm Hg, with a mean nocturnal dip of 17.9 ± 7.0/14.9 ± 4.8 mm Hg. The day-to-day variation in nocturnal BP dip averaged 6.0 ± 4.1 mm Hg for systolic BP (33% of the mean nocturnal dip) and 4.6 ± 2.8 mm Hg for diastolic BP (31% of the mean nocturnal dip). In multivariate regression analyses, variability in the BP dip was not related to age, gender, ethnicity, or body mass index, and reflected day-to-day variation in sleep BP more than variation in awake BP. The variability in nocturnal BP dip was predicted by day-to-day differences in the fragmentation index (for systolic BP dip, $P = 0.002$; for diastolic BP dip, $P = 0.042$), but not by day-to-day differences in daytime physical activity (for systolic BP dip, $P = 0.754$; for diastolic BP dip, $P = 0.083$).

In summary, in our cohort of generally healthy adults with an average nighttime BP dip of 17.9 ± 7.0/14.9 ± 4.8 mm Hg, the day-to-day variability in BP dip was substantial, averaging 6.0 ± 4.1/4.6 ± 2.8 mm Hg. The variability in BP dip was in part determined by day-to-day differences in sleep quality.

Keywords: Ambulatory blood pressure monitoring; Blood pressure dipping; Sleep quality

PO-283

USING TELEPHONIC OUTREACH TO IMPROVE BLOOD PRESSURE CONTROL

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The objective of the current study was to evaluate the effectiveness of a large scale telephonic outreach to improve blood pressure control among patients with hypertension in a large integrated health care system. Kaiser Permanente Southern California members >18 years identified in a hypertension registry with uncontrolled blood pressure were randomly assigned to an intervention group and a control group. The intervention group received an automated telephone call advising them to have a walk-in blood pressure check at their Primary Care Physician's office, followed a week later by a reminder telephone call. The control group received usual care. The primary outcome was blood pressure control (<140/90 mm Hg) at 4 weeks from initial contact. Both arms of the study occurred in an environment where primary care access was amplified by walk-in blood pressure checks and an aggressive hypertension treatment algorithm. Blood pressure control in the intervention and control groups at the time of randomization was 0%. Blood pressure control in the usual care group (n = 33,154) increased to 23.7% after 4 weeks. Blood pressure control in the intervention group (n = 33,150) increased to 31.9% after 4 weeks and was significantly different from the usual care group ($P < 0.05$). Of those patients with diabetes, blood pressure control in the usual care group (n = 8996) increased to 26.8% after 4 weeks and blood pressure control in the intervention group (n = 9040) increased to 34.0% after 4 weeks ($P < 0.05$ for usual care vs intervention). Of those patients with chronic kidney disease, blood pressure control in the usual care group (n = 3093) increased to 29.1% after

4 weeks and blood pressure control in the intervention group (n = 3176) increased to 35.0% after 4 weeks ($P < 0.05$ for usual care vs intervention). Within an integrated hypertension treatment program including walk-in blood pressure availability and a generally accepted medication titration algorithm, telephonic outreach appears to be an effective and efficient way to help improve blood pressure control in a large population of patients with hypertension. Further analyses may show that telephonic outreach is more effective for certain populations of patients with hypertension.

Keywords: Blood pressure control; Hypertension; Automated telephone outreach

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RELATIONSHIP BETWEEN THE REDUCTION OF LEFT VENTRICULAR MASS INDEX AND THE CHANGES IN SLEEP BLOOD PRESSURE WITH SODIUM RESTRICTION AND/OR DIURETIC TREATMENT

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Background: Sleep blood pressure and non-dipping (1-sleep SBP/awake SBP < 10%) are reported to be altered by sodium restriction and/or diuretics therapy; however, it is unclear whether the changes in sleep blood pressure and/or nocturnal dipping are associated with a reduction of left ventricular mass index (LVMI).

Methods: We evaluated 30 untreated hypertensive outpatients (clinic blood pressure≥140/90 mm Hg) in this study. Patients were instructed to decrease sodium intake (NaCl <6 g/day) for 8 weeks, and then prescribed indapamide 1 or 2 mg/day to control both clinic (<140/90 mm Hg) and home blood pressure (<135/85 mm Hg) for 4 months. The clinic and home blood pressure were measured monthly, and ambulatory blood pressure and an echocardiogram were performed at baseline and at the end of the treatment period.

Results: There were 12 non-dippers and 18 dippers. Sleep SBP/DBP decreased in both non-dippers (149 ± 19/81 + 16 to 126 ± 22/74 + 13 mm Hg, $P = 0.001$/ $P = 0.053$) and dippers (129 ± 9/81 + 8 to 121 ± 9/74 + 10 mm Hg, both $P < 0.01$). LVMI significantly decreased in non-dippers (116 ± 17.3 to 82 ± 27.8 kg/m^2, $P = 0.022$), but not in dippers ($P = 0.31$). In stepwise multiple regression analysis that considered the changes in clinic, morning home, evening home, awake, and sleep SBP and DBP, the changes in sleep DBP ($B = 1.17$, $P = 0.001$) and morning home SBP ($B = 0.43$, $P = 0.036$) were found to be significant predictors of percentage change in LVMI in non-dippers, while that in morning home SBP was significant in dippers ($B = 0.95$, $P = 0.016$). In the parallel analysis for 24-hour and dipping of SBP and DBP instead of awake and sleep SBP and DBP, the changes in dipping of DBP ($B = -1.74$, $P < 0.001$) and evening home DBP ($B = 1.25$, $P < 0.001$) were the significant predictors in non-dippers, while that in morning home SBP was significant in dippers ($B = 0.95$, 0.016).

Conclusion: The change in sleep DBP is a significant predictor of the percentage reduction of LVMI in non-dippers, and the change in morning home SBP is the significant predictor in both non-dippers and dippers.

Keywords: Salt restiction; Diuretics; Home blood pressure; Ambulatory blood pressure

PO-285

BpTRU – A USEFUL ALTERNATIVE TO 24 HOUR AMBULATORY BLOOD PRESSURE MONITORING IN EVALUATION AND MANAGEMENT OF HYPERTENSION IN INDIA

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Objective and Methods: Single clinic BP reading (CBP) is not always a satisfactory reflection of patients blood pressure control and 24 hour Ambulatory BP monitoring (ABPM) has its limitations. We were the first in India to utilize a new automated oscillometric office device called BPTRU. This device displays the average of 6 BP recordings taken in ideal setting over a period of 10 minutes at 2 minutes intervals. The Average BPTRU (RAV 2–6) is the average of last five readings, discarding the first reading (R1). This is a study of 100 consecutive patients correlating readings of BPTRU, ABPM and CBP to test the utility of BPTRU as a viable substitute to ABPM and CBP in hypertension management.

Results: The mean CBP [systolic = 152 ± 15.35, diastolic = 86.2 ± 9.58] was statistically different ($P = 0.01$ each) from the mean ABPM daytime systolic BP (128.9 ± 15.73) as well as diastolic BP (82.9 ± 8.99). The mean of RAV 2–6 [systolic = 127.9 ± 14.65, diastolic = 79.2 ± 9.34] however was not statistically different from the mean ABPM daytime readings ($P = 0.36$ and 0.26 respectively).

37/100 patients had either white coat hypertension or white coat effect (CBP > 140/90 with 24 hour ABPM and RAV 2–5 < 135/85) and in these patients, the mean R1 [systolic = 144.3 ± 18.14, diastolic = 84.8 ± 9.99] BP was not statistically different from the mean CBP readings ($P > 0.05$).

Using Pearson Correlation Coefficient, daytime Ambulatory BP correlated significantly better with RAV 2–6 than with CBP [$r = 0.81$ vs 0.51 for systolic and $r = 0.65$ vs 0.53 for diastolic BP respectively].

Conclusions: The BPTRU average better predicts the average daytime ABPM as compared to routine clinic BP measurements. BPTRU is also a very useful and cost effective alternative in assessment of White Coat Hypertension. This study also validates its utility in the management of difficult -to- control blood pressure in our patients.

Keywords: BPTRU; Ambulatory blood pressure monitoring; Sphygmomanometer; Clinic blood pressure

PO-286

WITHDRAWN AT AUTHORS' REQUEST

WITHDRAWN AT AUTHORS' REQUEST

PO-287

EFFECTS OF TRAFFIC-RELATED PARTICLES ON BLOOD PRESSURE AND DNA METHYLATION

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The mechanisms responsible for increasing blood pressure with exposure to airborne particulate have yet to be explained. This study examined how exposure to secondary traffic-related ambient particles affect blood pressure and investigates DNA methylation of the promoter of endothelial nitric oxide synthase (eNOS), a gene implicated in vasoconstriction.

Air from the plenum of a major tunnel exhaust stack in the northeastern US was drawn to a photochemical chamber used to mimic specific atmospheric conditions resulting in formation of traffic related secondary particles. Sprague Dawley (SD-CD) rats were exposed to either secondary traffic particles or filtered air. Primary and secondary pollutant gases were removed with a countercurrent denuder prior to animal exposures. Blood pressure measurements were collected for 12 days using a DSI PCA-40 implanted telemeter. Animals used in epigenetic analyses were exposed for 2 days and sacrificed 24 hours post exposure. DNA methylation anaylsis was performed using bisulfite sequencing on heart and lung tissue.

Diastolic and systolic blood pressure rose significantly on the first day of exposure, $P = 0.009$ and $P = 0.05$ respectively, and to a lesser extent on the second day, $P = 0.13$ and $P = 0.48$ respectively. Differences between exposed and control groups decreased with repeated exposures over time. A total of eight CpG sites were analyzed in the promoter region of the eNOS gene in both heart and lung tissue. Three of the eight sites in lung tissue were significant for differences in mean percent DNA methylation between exposed vs unexposed ($P < 0.05$) while an additional lung CpG site was borderline significant ($P = 0.06$). Only one site was significant for the heart. Overall trends indicate a decrease in DNA methylation across sites for both tissue types.

The decrease in differences in blood pressure with repeated exposures over time suggests a compensatory response to particulate exposures. While the DNA methylation data is a cross-sectional sample, the decrease in DNA methylation in the eNOS promoter suggests the activation of the gene resulting in potential vasodilatory effects as validation of this compensatory response.

Keywords: Particulate matter; Blood pressure; DNA methylation

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AMBULATORY BLOOD PRESSURE IN THE BIOLOGICAL TIME STRUCTURES

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Monitoring biological time structures (such as yearly rhythm: circannual, about-weekly: circaseptan and circadian) are considered essential parameters to recognize and treat any risk elevation as well as overt disease. Blood pressure (BP) and heart rate (HR) in adolescents and adults were monitored around the clock at 30-minute to hourly intervals for years, and analyzed by the cosinor method. All showed significant circadian fluctuations in BP and HR. BPs showed about 10–20 mm Hg higher in the adult group while HR was lowered in about 10 beats/min. The circadian response peaked at noon to the late afternoon hours: SBP: -272°(18:08); DBP: -257° (17:08); HR: -265° (17:40) with 360°= 24 hours), in keeping with the impression from the five adult subjects, individual differences notwithstanding, while one teen showed shift changes to the early morning hours: SBP: -27° (01:48); DBP: -21° (01:24): HR: -2° (00:12). Circannual data revealed significant rhythms in BP and HR with peaks on October 27 (SBP: -295°), November 26 (DBP: 324°) and October 31 (HR: -299°). The winter month BP and HR were the lowest in four seasons: Spring, Summer, Fall and Winter: 110.9 ± 2.9; 110.4 ± 1.3; 115.2 ± 1.3; 96.0 ± 5.1 for SBP; 70.5 ± 1.2; 71.4 ± 0.5; 77.4 ± 0.6; 59.7 ± 2.0 for DBP in mm Hg; and 61.1 ± 0.9; 60.0 ± 0.4; 60.4 ± 0.4; 48.7 ± 1.2 beat/min for HR, respectively. Sudden drops of both BP and HR were noted at the point of surgery in late January. SBPs were significantly elevated during initial 3-year undergoing recovery from severe spine-vertebrate injuries than those of later 2-year recovery periods ($P < 0.01$), while DBP and HR ranged various. Sharp increased circadian double were observed in the winter season amplitudes (SBP 72.6 ± 6.1; DBP 35.4 ± 2.9; HR 23.8 ± 1.8, all $P < 0.0001$). Circaseptan double amplitudes in the adolescents were 12.5 ± 4.1 ($P = 0.019$) for SBP and 7.8 ± 2.8 mm Hg ($P = 0.030$) for DBP, with acrophases occurring on late Sunday, early Monday (at 50° and 67° from 00:00 on Saturday to Sunday for SBP and DBP, respectively, with 360°=1 week). Increased amplitude can be a greater risk than MESOR-hypertension and circaseptan acrophases coincide with

the times of increased morbidity/mortality from vascular diseases demonstrated in our studies. Time structures broader than circadian should be considered in interpreting BP responses as a gauge of vascular disease status.

Keywords: Ambulatory blood pressure; Circadian BP overswinging; Vascular disease risk; Morbidity and mortality

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AMBULATORY BLOOD PRESSURE MONITORING IN HYPERTENSIVE SMOKERS: EVIDENCE OF IMPAIRED NIGHT-RESPONSE

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Smoking (S) and hypertension (H) are major risk factors for cardiovascular disease. In addition, there is evidence that non-dipper hypertensive individuals are at increased cardiovascular risk. The purpose of this study is to investigate the response to 24-hour Ambulatory Blood Pressure Monitoring (ABPM) of hypertensive smokers.

Material and Method: Study material comprised 104 hypertensive men aged from 55 to 72 years (mean: 63 ± 8 years), 72 smokers (69%) and 32 non-smokers (31%), used as a control group, undergone 24-hour ABPM. Mean day systolic blood pressure (BP) was 162 (±18) mm Hg and diastolic BP 92 ± 7 mm Hg for smokers group and 159 ± 17 mm Hg for systolic BP and 94 ± 6 mm Hg for diastolic BP in non-smoker control group. Statistical analysis was conducted and a P values <0.05 were statistically significant.

Results: Forty-eight hypertensive smokers (67%) were non-dippers for systolic BP (night BP reduction from 0% to 7%) while the other 33% (24 patients) were dippers with a BP reduction from 10% to 13%. Diastolic reduction was from 3% to 8% in 39 smoker patients (54%) and from 12% to 14% in the others. On the contrary, among hypertensive non-smokers, there were 26 dippers (81%) for systolic BP with a reduction from 12% to 15% and 24 (75%) for diastolic BP (reduction from 10% to 14%), and 6 (19%) non-dippers with a systolic and diastolic BP reduction from 4% to 9%. Statistical difference ($P < 0.05$) existed between non-dipper smokers and dipper non-smokers as well as between non-dipper and dipper smokers particularly for systolic BP values.

Conclusions: In this study hypertensive smokers are more frequently non-dippers particularly for systolic values of BP, and this pattern identifies possibly more extended cardiovascular system damage caused by the association of S with H.

Keywords: Blood pressure monitoring; Hypertension; Smoking; Dippers non-dippers

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OSCILLOMETRIC AND AUSCULTATORY BLOOD PRESSURE MEASUREMENTS BEFORE AND AFTER ACUTE EXERCISE AND REST IN THE ELDERLY

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The objective of this study was to compare blood pressure (BP) values obtained by auscultatory and oscillometric methods before and after a session of aerobic exercise and rest in the elderly. The oscillometric method could be useful in assessing blood pressure (BP) before and after exercise, especially when there is external noise, lack of professional training for the correct BP measurement by auscultatory method, and to avoid mercury poisoning.

All 23 elderly volunteers participated in a single exercise session (ES) (walk) and a resting control session (CS), according to previous randomization. The sessions were held at one week intervals. The session started with 20 minutes of BP measurements, with the auscultatory (mercury sphygmomanometer) device installed on the right arm and the oscillometric (Omron-HEM-431) device on the left arm. The two devices were insufflated simultaneously every 5 minutes.

At the end of the sessions, the participants sat down, the devices were installed and BP was measured over an additional period of 60 minutes, every 5 minutes.

Mean age was 67.7 ± 3.5 years, with 16 female gender volunteers, 11 treated hypertensive patients (HT), and 12 normotensive ones (NT). Comparisons between methods are shown in Table I.

In conclusion, there was good agreement for systolic BP between auscultatoty and oscillometric methods, except after exercise. This method can be useful to evaluate older hypertensive individuals before exercise.

Table I. Degree of agreement (coefficient of St. Laurent) between auscultatory and oscillometric methods before and after the sessions (exercise and rest)

Session	Variable	Coefficient	CI (95%)
Before rest	SBP	0.70	(0.48; 0.86)
Before rest	DBP	0.61	(0.42; 0.80)
After rest	SBP	0.83	(0.69; 0.93)
After rest	DBP	0.59	(0.41; 0.77)
Before exercise	SBP	0.80	(0.62; 0.91)
Before exercise	DBP	0.72	(0.60; 0.83)
After exercise	SBP	0.68	(0.44; 0.86)
After exercise	DBP	0.72	(0.58; 0.84)

Keywords: Elderly; Exercise; Auscultatory method; Oscillometric method

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HOME BLOOD PRESSURE MONITORING REQUIRES FEEDBACK TO PATIENTS TO IMPROVE TREATMENT OF HYPERTENSION

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Background: Several national and international guidelines recommend incorporating home blood pressure monitoring (HBPM) into the routine management of hypertensive patients. Yet, the evidence that HBPM improves blood pressure (BP) control is weak. This study assessed whether HBPM on its own (no feedback) or linked to a telemonitoring system that provided feedback to patients improves BP control.

Method: In a randomized controlled trial, 110 diabetic patients with uncontrolled systolic hypertension were randomly assigned to monitor their BP at home without feedback or to the HBPM system that automatically, using pre-programmed algorithms, provided action messages and measurement reminders (no vetting by a health professional). All patients were taught one-on-one

how to measure their BP correctly and the recommended frequency of measurement per week, and were given a validated home BP measuring device. The non-feedback group was instructed on the meaning of the BP readings and what to do if the readings were too high or low. All care was delivered by the patients' own physician.

Results: In the non-feedback group, there was no within group change in 24-hour ambulatory BP monitoring (ABPM) or 7-day self-monitoring of BP from baseline to outcome 1 year later. However, in the feedback group, there was a highly significant within-group fall in BP, and the differences in the fall of BP in the feedback vs non-feedback group were 6.8 ± 2.4 mm Hg (mean ± SE) for systolic BP and 3.6 ± 1.3 mm Hg for diastolic BP ($P < 0.006$) on 24-hour ABPM and 9.0 ± 2.4 for systolic BP and 4.0 ± 1.3 for diastolic BP ($P < 0.004$) on 7-day self-monitoring of BP. Furthermore, BP control on 24-hour ABPM was also significantly better (50% in feedback group vs 29% in non-feedback group, $P < 0.05$). There was no significant between-group change from baseline in the number of antihypertensive drugs per patient or difference in the number of doctor visits in the study year.

Conclusion: HBPM that does not provide feedback to hypertensive patients is ineffective in improving BP control.

Keywords: Hypertension; Telemonitoring; Diabetes; Blood pressure control

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BLOOD PRESSURE IN FIREFIGHTERS

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Background: The prevalence of hypertension (HTN) is rising in the United States where nearly one-third of adults have HTN and many are either unaware of their disease or it is uncontrolled. Among firefighters, approximately 75% have uncontrolled HTN compared to 55% in the general US population. The Stop, Drop and Control (SDC) Program is designed to help firefighters control their blood pressure and cardiovascular risk. The objective of this research was to characterize the firefighter population for HTN and blood pressure (BP) levels and establish the baseline before implementation of the SDC program.

Methods: Retrospective analysis of medical examination reports, required by the Indianapolis Fire Department (IFD), was conducted among a random sample of firefighters. Extracted medical examination data included BP, body mass index (BMI), body fat, demographic information, and patient-reported medical history and medication use. Guidelines issued by the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (HBP) were used to classify firefighters' hypertensive status.

Results: Health data from a total of 505 IFD firefighters were included, representing approximately 48% of the 1050 IFD firefighters. The mean age of the firefighters is 43.5 years (24–69) and 95% of the firefighters are male. More than half (56%) of the IFD firefighters are pre-hypertensive, and two-thirds (68%) are either pre-hypertensive or hypertensive. As such, compared to the Kales et al 2009, a review of BP levels among emergency responders, significantly fewer IFD firefighters are classified with HTN (12% vs 21%, $P < 0.001$) and more have a normal BP (32% vs 21%, $P < 0.001$) –this is mainly attributed to IFD's extensive wellness fitness initiative. However, among the IFD firefighters with HTN (12%), only 36% reported taking HTN medications.

Conclusions: Steps can be taken now – such as education, awareness, and the adoption of a healthy lifestyle – to assist in the prevention of HBP among pre-hypertensive firefighters, and to control HBP among the firefighters with HTN. Further investigation is warranted to assess the clinical impact post implementation of the SDC Program.

Keywords: Hypertension; Firefighters; Blood pressure; Stop drop control program

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LONG-TERM EFFECTS OF TELEMETRIC BLOOD PRESSURE MONITORING IN ADEQUATELY TREATED PATIENTS WITH ARTERIAL HYPERTENSION

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Background and Aim: Studies confirm that an optimized blood pressure (BP) adjustment, compared to a standard attended control-group, can be achieved with the help of a 3-month telemetric blood pressure measurement (TBPM) in inadequately treated patients with arterial hypertension. This recent analysis should clarify if these effects lead to a better control in the middle and in long term.

Methods: Fifty-seven patients (including three dropouts) with initially inadequately treated arterial hypertension were evaluated in the former intervention study concerning BP adjustment after 3 month of TBPM (besides standard supply the TBPM group was supported additively by a telemetry supply for the daily transfer of the measured BP values at home to the physician. In case of an insufficient BP-control or non-compliance, the physician was able to counteract for example in form of changing medication or intervention via phone).
In conclusion an ABPM could be carried out with 18 (TBPM) and 22 patients (controls), respectively, after a period of 617 and 576, respectively, days on average.
Those patients were compared concerning BP-target values (ABPM > 130/80 or >125/75 mm Hg with diabetes/renal failure) with the terminal data after the initial 3-month BP adjustment period.

Results: After a 3-month experimental period significantly more percent of those patients belonging to the TBPM group achieved the asked target values than those ones belonging to the control group (TBPM: 54%, controls: 36%; $P = 0.007$). A similar distribution was also confirmed after 617 and 576 days, respectively (TBPM: 56%, controls: 40%; $P = 0.024$).

Conclusion: TBPM allows not only an optimized BP control during the initial 3-month BP adjustment in patients with inadequately treated arterial hypertension, it also allows a better adjustment of BP target values compared to standard supply in the long term. Interventional TBPM creates a long time effect by an optimized therapy adjustment in the titration period and on the other hand by an amelioration of patient compliance in the long term.

Keywords: Hypertension; Telemedicine; Telemetry; Diagnosis of hypertension

PO-294

RELATIONSHIP BETWEEN CENTRAL AND PERIPHERAL BLOOD PRESSURE IN TYPE 2 DIABETIC AND PREDIABETIC PATIENTS

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Impaired glucose homeostasis is associated with arterial stiffness, but whether this differs on peripheral or central BP is unknown. We aimed to assess the relationship between different estimates of both peripheral BP (office BP, 24 hour-, day-, and night- BP) and central BP in patients with impaired glucose metabolism.
Cross-sectional study in subjects with DM2 or pre-diabetes ($\geq$3 of the following: TG > 150 mg/dL or drug therapy; HDLc <40 mg/dL in men (M) or <50 mg/dL in female (F) or drug therapy; waist circumference >88 cm (F) or >102 cm (M); plasma fasting glucose >100 mg/dL or drug therapy; BP $\geq$130/85 mm Hg or antihypertensive treatment). Demographic and antropometric data, laboratory analyses and EKG were recorded. Office BP, 24 hour-ABPM and central BP by radial artery applanation tonometry (Sphygmocor®) were measured.
N = 506 patients (DM2 75%; pre-diabetics 25%); age 64 ± 10 year; M/F: 62%/38%; BMI 30.9 ± 4.3 kg/m^2; waist circumference 106 ± 10 cm (M), 103 ± 11 (F). Other risk factors: hypertension 91%; dyslipidemia 72%; smokers14%.
Office BP (mm Hg): SBP 142.3 ± 20.9; DBP 80.5 ± 12.3.
ABPM (mm Hg): 24 hour-SBP: 127.4 ± 14.5; 24 hour-DBP: 72.9 ± 9.1; day-SBP: 130.4 ± 15.0; day-DBP: 75.7 ± 9.6; night-SBP: 120.4 ± 16.1; night-DBP: 66.6 ± 9.3.
Central BP (mm Hg): cSBP: 127.4 ± 19.5; cDBP: 80.0 ± 12.6; cPP: 47.6 ± 15.2. AIx: 30.3 ± 11%.

Pearson's "*r*"	Central SBP		Central DBP
Office-SBP	0.768	Office-DBP	0.818
24 hour-SBP	0.579	24 hour-DBP	0.602
Day-SBP	0.589	Day-DBP	0.610
Night-SBP	0.768	Night-DBP	0.610
$P < 0.001$ for all correlations			

Correlations between central and peripheral BP: ROC curves were performed to determine the thresholds of central BP better correlated to normal ranges of the different peripheral BP measurements. The threshold for central SBP better associated with clinic hypertension is 121 mm Hg, with very high sensitivity and high specificity. Obtained cutoffs for ABPM estimates showed less sensitivity and specificity.
In diabetic and pre-diabetic subjects, the best correlations of non-invasively determined central BP were with office BP as compared to other peripheral BP estimates. Central SBP of 121 mm Hg is the threshold that better discriminates the presence of hypertension diagnosed by office BP assessment.

Keywords: Central blood pressure; Type 2 diabetes; Pre-diabetics; ABPM

PO-295

CLINICAL CHARACTERISTICS, BLOOD PRESSURE (BP) CONTROL, AND ANTIHYPERTENSIVE TREATMENT (TRX) PATTERNS AMONG ELDERLY PATIENTS (PTS) WITH HYPERTENSION (HTN)

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Objective: To examine the clinical characteristics, trx patterns, and rate of BP control among elderly HTN pts.

Methods: A retrospective open-cohort medical records review was conducted across four primary care centers in the United States. Pts were $\geq$65 years (year), had a confirmed diagnosis of HTN on the 1st visit on or after 01/01/2007 with $\geq$1 BP reading, and $\geq$1 follow-up visit. Pts were excluded if they had a history of HTN emergency, terminal illness, or were institutionalized. Pts were randomly chosen from a list of potential pts. The observation period began on 1st visit and ended at earliest date among date of last clinic visit, death, or chart abstraction. Follow-up visits were recorded in 3 month intervals. Pts were categorized as: no relevant conditions (e.g. high coronary disease [HCD] risk) or compelling indications (e.g. diabetes mellitus [DM]) (0-RCCI), 1-RCCI, and $\geq$2-RCCI, per JNC-7 guidelines. Descriptive analysis was conducted using ANOVA and chi-squared test.

Results: Three hundred and fifty-seven patients were included: 68 (0-RCCI), 132 (1-RCCI), 157 ($\geq$2-RCCI). Mean age of the sample was 78.3 (±7.0) year and similar across groups. 72.8% of pts had HCD risk. 96.1% of pts were prescribed anti-HTN medications (med) at 1st visit; 66.5% of those received combination therapy. Use of anti-HTN med classes by RCCI was consistent per JNC-7 guidelines except for stroke (only 43% of pts received recommended med classes) and DM (only 34% and 34% received diuretics and angiotensin converting enzyme inhibitor/angiotensin receptor blocker med classes, respectively). $\geq$1 trx modification was observed for: $\geq$2-RCCI (61.8%), 1-RCCI (57.6) and 0-RCCI (55.9%) pts. Pts with $\geq$2-RCCI had higher mean systolic BP at 1st visit (141.2 mm Hg) compared to 0-RCCI (131.4) and 1-RCCI (137.4) ($P < 0.001$). Frequency of BP goal attainment per JNC-7 was lower in pts with $\geq$2-RCCI with 15% of $\geq$2-RCCI pts achieving BP goal in more than 75–100% of visits with BP measurements while the proportions increase to 50% and 33% for pts with 0 and 1 RCCI, respectively ($P < 0.001$).

Conclusion: Pts with higher RCCI had a significantly lower rate of BP goal attainment over time supporting the need for more aggressive HTN management in elderly pts.

Keywords: Hypertension; Elderly; BP control; Treatment patterns

PO-296

PROGNOSTIC VALUE OF REPEATED AMBULATORY BLOOD PRESSURE MONITORING IN REFRACTORY HYPERTENSION

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Objective: The objective was to assess whether or not repeated ambulatory BP values throughout a long follow-up period

represent a more accurate prognostic tool than office BP in evaluating resistant hypertension.

Subjects and Methods: The inclusion criteria were: (a) office BP > 150/95 mm Hg for three visits at 1-month intervals during the same antihypertensive treatment, which included three or more antihypertensive drugs, one of them being a diuretic. Patients with secondary hypertension or GFR > 45 mL/min/1.73 m^2 were excluded. A minimal 6-month of follow-up was required for being included in the analysis. Ambulatory BP monitoring of 24 hours was performed at the beginning and every 2 years until events occurs or until the final examination. The incidence of new cardiovascular events (myocardial infarction, coronary revascularization, stroke, transient ischemic attack, sudden death and new occurrence of heart failure), fatal and nonfatal, was collected during the follow-up. Cox time-varied proportional hazard model was used.

Results: Eight hundred and ninety-eight ABPM were performed in 386 patients. For the analysis only the 32 first events, 2.5 events per 100 patients-year, were considered. While initially no differences in office systolic or diastolic BP were observed between patients with or without events, patients with events had significantly higher values of ambulatory BP, mainly at night. At the time of the last examination, subjects who are going to develop events had significantly higher values of 24-hour, daytime and nighttime systolic BP while no differences were present in office BP. When a multivariate analysis was performed, previous cardiovascular events [RR 7.35, (6.75–27.1, 95% CI)] and fasting glucose values >110 mg/dL [RR 2.72, (1.37–6.78, 95% CI)] remained as independent significant factors. When all the other variables were included only 24-hour systolic BP > 135 mm Hg became also independently significant [RR 2.04, (1.03–4.33, 95% CI)] associated to the risk of events.

Conclusions: Average of 24 hours ambulatory systolic BP repeated overtime had an independent prognostic value for the development of cardiovascular events in a cohort of refractory hypertension. The prognostic value was on top of repeated office BP values.

Keywords: Refractory hypertension; 24 hour ABPM; Prognosis

PO-297

ANTIHYPERTENSIVE EFFECTIVENESS OF COMBINATION LERCANEDIPINE WITH DILTIAZEMI IN PATIENTS WITH MILD TO MODERATE ARTERIAL HYPERTENSION

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The aim was to evaluate the antihypertensive effects combination lercanedipine with diltiazemi in patients with mild to moderate arterial hypertension.

Patients and Methods: Twenty-seven patients were included. Systolic (SBP) and diastolic (DBP) blood pressure, heart rate, patient's compliance, adverse reactions, efficacy of therapy baseline and 1 month of treatment were evaluated. Ambulatory blood pressure monitoring and central blood pressure were done in all patients before and on 1st month of therapy. Combination lercanedipine 20 mg with diltiazemi 240 mg daily dose. Mean age of patients was 53.5 ± 0.96 year, BMI – 31.44 ± 0.46 m^2, initial SBP – 163.75 ± 0.65 mm Hg, DBP – 95.83 ± 0.73 mm Hg., heart rate – 77.42 ± 0.53 b.m.

Results: That was established that in mild and moderate hypertensive patients. combination lercanedipine 20 mg with diltiazemi 240 mg decreased the office SBP from – 163.75 ± 0.65 to 148.33 ± 0.45 mm Hg, ($P < 0.05$) and DBP from – 95.83 ± 0.73 to 83.33 ± 0.35 mm Hg, ($P < 0.05$) heart rate was not significant change – from 77.42 ± 0.53 to 75.67 ± 0.33 b.m. ($P > 0.05$). The average daily decreased the SBP from – 145.66 ± 0.54 to 128.47 ± 0.49 mm Hg, ($P < 0.05$) and DBP from – 86.23 ± 0.63 to 80.16 ± 0.39 mm Hg, ($P < 0.05$) heart rate was not significant change – from 71.32 ± 0.51 to 73.13 ± 0.30 b.m. ($P > 0.05$). Central blood pressure decreased from – 139.75 ± 0.44 to 129.50 ± 0.55 mm Hg, ($P < 0.05$) We did not note any negative changes in biochemical and clinical laboratory data. Only five adverse events were noted (edema, tremor hand to lercanedipine and headache, stuffiness in ear, flushing to diltiasemi,) and only in one cased (edema, tremor hand) it was needed to stop lercanedipine and one cased (headache, flushing) it was needed to stop diltiasemi.

Conclusion: The combination lercanedipine with diltiazemi therapy was effectiveness, safety and well tolerated.

Keywords: Arterial hypertension; Lercanedipin; Diltiasem; Treatment

PO-298

HIGHER NIGHT-TIME BLOOD PRESSURE AND CARDIAC DAMAGE IN 1176 PATIENTS: EFFECTS OF BMI AND DRUG THERAPY

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Evaluation of the relationship between BMI, ambulatory blood pressure (ABPMonitoring, Spacelabs 90207) blood pressure, and cardiac organ damage by retrospective study on 1776 outpatients (after exclusions because unreliable ABPM) referred to our centre for 24 hour BP and cardiac organ damage evaluation. Treatment Intensity Score (TIS) was calculated and used to adjust results. According to BMI, there were no significant differences in mean 24 hour and daytime SBP and DBP between normal weight (n = 575), overweight (n = 772) and obese patients (n = 429), also after adjustment for sex, age and TIS. On the other hand, mean night-time SBP increased significantly from normal weight (SBP = 122.5 ± 15.1 mm Hg) to overweight (SBP = 123.9 ± 15.4 mm Hg) and to obese patients (SBP = 125±15.9 mm Hg) ($P = 0.044$) with a parallel increase in night-time pulse pressure (from 50.7 to 51.3 to 52.4 mm Hg respectively; $P = 0.05$). Higher night-time SBP was associated also with higher prevalence of non dipper and reverse dipper profiles. Obese subjects had a higher TIS (TIS = 1.35) compared to overweight (TIS = 1.22) and normal weight patients (TIS = 1.1) ($P < 0.001$). After dividing the sample for the presence/absence of therapy, night-time BP differences emerged only in hypertensive patients untreated or not controlled, while there were not significant differences between normotensive subjects or controlled Echocardiografic parameters such as left atrial diameter, LVM/$h^{2.7}$, LVEF and E/A ratio worsened from normal weight to overweight and obese patients. Only not-controlled hypertensive subjects and untreated hypertensives had significantly lower LVEF and E/A ratio correlated with higher BMI. Increasing adiposity is associated with a worsening of night-time blood pressure and higher prevalence of non dipper and reverse dipper patterns. Obesity is also associated with a worsening in cardiac function indexes and with cardiac organ damage. This is especially evident in untreated and in not controlled hypertensives. Appropriate pressure control is not associated with increased night-time BP and cardiac damage

despite increasing BMI. The evidence of a higher night-time SBP in obese patients, despite higher TIS indicate also that obesity is associated to a relative resistance to antihypertensive treatment.

Keywords: Ambulatory blood pressure monitoring; Hypertension; Obesity; Drug therapy

PO-299

SEASONALITY OF 24 HOUR, DAYTIME AND NIGHT-TIME BLOOD PRESSURE: SUMMER DOES NOT ALWAYS MEANS LOWER

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We investigated the effects of different seasons on 24 hour, daytime, and night-time blood pressure using the data from 4503 ambulatory blood pressure monitoring (ABPM, Spacelabs 90207) of patients referred to our Hypertension Center between September 2002 and August 2010. Exclusion critera were: age <18 years, low-quality pressure monitoring, and unreliable data regarding anti-hypertensive treatment. Population was divided by age (younger <65 years of age and elderly ≥65 years of age), by sex, and in treated/untreated subgroups.

As expected, mean 24 hour and daytime systolic (SBP) and diastolic blood pressure (DBP) were higher in winter (130.4 ± 13.9/79.3 ± 10.3 mm Hg for the 24 hour, 133.8 ± 14.0/82.5 ± 10.6 mm Hg for daytime) and lower in summer (128.6 ± 13.0/77.6 ± 9.8 mm Hg for 24 hour, 130.9 ± 13.1/80.0 ± 10.0 mm Hg for daytime) ($P < 0.001$) compared with autumn and spring when blood pressure values were not significantly different from others, even after adjusting for sex, age and treatment. However, the highest night-time mean SBP was recorded in summer and was significantly different even vs the winter season (123.3 ± 14.5 vs 122.0 ± 15.4 mm Hg in winter) ($P = 0.01$) although seasonal differences were less pronounced. This results were confirmed for both treated and untreated subgroups, as well as controlled or uncontrolled patients and younger or elderly.

Our data on a very large ABPM sample confirm the findings of previous scientific studies concerning the relationship between seasons and 24 hour-daytime ambulatory blood pressure. However, the finding of an inverse relationship between the hottest and coldest seasons regarding night-time BP was quite unexpected and might be related to different sleeping behaviors between summer and the other seasons. These data are especially important as night-time BP could become a new therapeutic target.

Keywords: Ambulatory blood pressure monitoring; Hypertension; Drug therapy; Seasonal blood pressure modification

PO-300

IMPROVEMENT IN HYPERTENSION CONTROL AFTER A 2-YEAR PARTICIPATION IN A WEB-BASED PROGRAM ON HIGH BP MANAGEMENT

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Our aim was to evaluate changes in hypertension control reported by physicians participating in a web-based project for management of patients with high BP.

We selected physicians participating in the Spanish Society of Hypertension ABPM Registry, each one recruiting >20 subjects both in 2005 (group 1 or G1) and 2007 (group 2 or G2) (n = 71). Data between both groups were compared. Cases with repeated ABPM were discarded. Office BP was considered as controlled when <140/90 mm Hg and ambulatory BP was considered as controlled when 24-hour BP <130/80 mm Hg.

G1 and G2 included 4158 and 3253 patients respectively. Age (62.3 vs 62.7 years), duration of hypertension (8.3 vs 8.1 years), body mass index (29.5 vs 29.3 kg/m^2), presence of at least one additional cardiovascular risk factor (91.1% vs 90.3%), prevalence of diabetes (21.9% vs 20.7%), and prevalence of established cardiovascular disease (16.8 vs 15.6%) were similar in both groups. Male sex was 49.0% in G1 and 51.6% in G2, $P = 0.03$. Office BP was 151.2/86.6 mm Hg in G1 and 146.8/84.2 mm Hg in G2 ($P < 0.001$), and control rates were 22.8% and 27.9% respectively ($P < 0.001$). Mean 24-hour BP was 130.4/75.4 mm Hg in G1 and 129.2/74.7 mm Hg in G2 ($P < 0.01$), and ambulatory control rates 45.1% and 48.0% respectively ($P = 0.022$). Combination antihypertensive therapy was more frequently used in 2007 (68.5%) than in 2005 (63.3%), $P < 0.001$. In conclusion, modest improvement in 2-year hypertension control rate was observed in patients attended by participant physicians in this web-based ABPM registry. Programs designed to help physicians in daily management of hypertensive patients may be useful for ameliorating hypertension control.

Keywords: Ambulatory blood pressure monitoring; Blood pressure control; Spanish society hypertension ABPM registry; Web-based project

PO-301

AMBULATORY BLOOD PRESSURE MONITORING IN PREHYPERTENSION

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Background: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) introduced prehypertension as a new classification of blood pressure. The non-dipping status is frequently in hypertension. Prehypertensive individuals are at increased risk for developing hypertension and cardiovascular disease.

Objective: The purpose of our study was to evaluate the 24-hour ambulatory blood pressure (ABP) and circadian blood pressure (BP) rhythm in patient with prehypertension.

Methods: We studied 223 patient 125 men, aged 18–71 years (mean 45.06 ± 6.45). The office blood pressure of these patients was determined as prehypertension (systolic blood pressure 120–139 or diastolic 80–89 mm Hg.) After the diagnosis of prehypertension we performed 24 hour ambulatory blood pressure monitoring.

Results: The office systolic blood pressure was 124.52 ± 14.31 mm Hg and diastolic was 82.38 ± 14.31 mm Hg. After the identification of prehypertension the patients were investigated by 24-hour ambulatory blood pressure monitoring system. The average systolic ambulatory blood pressure was 112.77 ± 10.34 mm Hg and diastolic was 70.83 ± 8.17 mm Hg. The systolic nocturnal blood pressure fall was abnormal (non-dipper) 9.38 ± 7.01%. The mean body mass index was in the overweight category 25.70 ± 3.63 kg/m^2. The mean serum total cholesterol level was 6.06 ± 1.49 mmol/L, the LDL-cholesterol level was

3.11 ± 1.49 mmol/L, the HDL-cholesterol level was 0.89 ± 0.22 mmol/L and the triglycerides level was 2.80 ± 2.42 mmol/L. The mean fasting glucose (5.06 ± 0.79 mmol/L) the creatinine (101.43 ± 10.88 mmol/L), the urea nitrogen (5.76 ± 1.36 mmol/L) and the uric acid (308.67 ± 81.87 mmol/L) levels were normal.

Conclusions: These findings suggest that patients with prehypertension have abnormal systolic nocturnal BP fall and BMI, lipid parameters that risk factor for target organ damage and cardiovascular diseases. The prehypertension does not exclude the normal 24-hour ambulatory blood pressure values.

Keywords: Ambulatory blood pressure; Circadian rhythm; Hypertension; Prehypertension

PO-302

DIAGNOSTIC ACCURACY OF HOME VS AMBULATORY BLOOD PRESSURE MONITORING

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Assessment of out-of-office blood pressure (BP) using 24-hour ambulatory BP (ABP) monitoring is regarded as a valuable tool for the accurate diagnosis of hypertension and the detection of the white coat (WCH) and masked hypertension (MH) phenomena. Self monitoring of BP by patients at home (HBP) is an alternative method for the evaluation of out-of office BP. This study investigated the diagnostic accuracy of HBP compared to ABP monitoring in subjects attending a BP clinic. Baseline predictors of WCH and MH were also investigated. A total of 613 untreated and treated subjects were included (mean age 53 ± 12.4 [SD] years, 57% male, 59% untreated). Clinic BP was measured in three visits within 6 weeks. Within the same period HBP (6 days, duplicate morning and evening measurements) and awake ABP monitoring (at 20 minutes intervals) were performed in random order using validated oscillometric devices. Clinic BP (140 ± 15/89 ± 11 mm Hg, systolic/diastolic) was higher than HBP (136 ± 14/85 ± 10 mm Hg, $P < 0.001$) and awake ABP (137 ± 14/87 ± 11, $P < 0.001$). There was no difference between systolic HBP and awake ABP, yet diastolic HBP was lower ($P < 0.001$). Sustained hypertension was diagnosed by ABP in 65% and by HBP in 66% (agreement 77%, κ 0.49), WCH in 14.4% and 13.9% respectively (agreement 89%, κ 0.56) and MH in 15.3% and 15.3% (agreement 88%, κ 0.52). By taking ABP as the reference method, the sensitivity, specificity, positive and negative predictive value of HBP in detecting sustained hypertension were 83%, 66%, 82% and 67% respectively, WCH 61%, 94%, 64% and 94% and MH 60%, 93%, 60% and 93%. MH was more common in treated patients (23% by HBP; 20% by ABP) than in untreated (10% by HBP; 12% by ABP, $P < 0.05$/ = NS compared to treated). Using ABP or HBP, female sex was associated with higher risk of WCH, whereas an increasing clinic pulse pressure (CPP) was positively accociated with WCH by ABP. Treatment of hypertension, age and a decreasing CPP were independent predictors of MH by HBP, whereas treatment of hypertension, a decreasing CPP and a decreasing heart rate by ABP. These data suggest that HBP is a reliable alternative to ABP in the evaluation of out-of-office BP and the detection of the WCH and MH phenomena.

Keywords: Ambulatory blood pressure monitoring; Home blood pressure monitoring; Masked hypertension; White coat hypertension

PO-303

PATIENTS' PREFERENCE FOR OUT-OF-OFFICE BLOOD PRESSURE EVALUATION METHOD: AMBULATORY OR HOME MONITORING?

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Patient's preference and satisfaction might improve compliance to antihypertensive treatment and long term blood pressure (BP) control. This study aimed to compare patient's preference in using two different methods for out-of-office BP monitoring. Subjects referred for hypertension, were evaluated with ambulatory BP monitoring (ABPM) (measurements at 20 minutes intervals for 24 hours) and home BP monitoring (HBPM) (duplicate morning and evening measurements for 7 days) using validated oscilometric devices in random order within 2 weeks. Participants filled a questionnaire including demographics, previous experience in BP measurement methods and likert scale based questions on patient's acceptance, preference, disturbance, activities' restriction and feasibility of ABPM and HBPM. A total of 143 patients were invited and 104 (70%) agreed to participate (mean age 51 ± 11 years, 58% men, 75% untreated, 22% smokers, 38% working full time, 66% with >12 years of education, 50% employees, 28% self-occupied). A total of 62% of the participants considered ABPM as more reliable than HBPM, yet 60% would choose HBPM for their next BP evaluation. Eighty-three percent reported a positive overall opinion for HBPM vs 63% for ABPM ($P < 0.05$). Moderate to severe disturbance from using ABPM was reported by 55% and severe restriction of their daily activities by 30%, compared to 13% and 7% respectively from using HBPM ($P < 0.05$, for both comparisons). Neither cluster of demographics nor history of BP measurements was found to be an independent predictor of patients' preference. These data suggest that HBPM performs significantly better than ABPM in the overall acceptance and preference by hypertensive patients. Further studies are needed to incorporate patient's preference in routine medical decisions in clinical practice.

Keywords: Patient's acceptance; Home blood pressure monitoring; Ambulatory blood pressure monitoring; Patient's preference

PO-304

PREDICTIVE VALUE OF AMBULATORY BLOOD PRESSURE FOR CARDIOVASCULAR EVENTS IN HYPERTENSIVE PATIENTS AFTER A FIRST EVENT

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Introduction: It is still uncertain whether in hypertensive patients a 24-hour ambulatory blood pressure (ABP) performed after first cardiovascular (CV) event predicts the occurrence of new CV event.

Methods: ABP was performed in 235 hypertensive patients (61.1 ± 9.5 years, 61 women. BMI 28.8 ± 3.9 kg/m^2). Occurrence of new CV events was followed for 4.2 years (0.2–12.8) for 981 patients-years under stabilized antihypertensive medication.

Results: There were 59 new CV fatal/non-fatal events (25 strokes, 22 coronary, 12 other CV events). At baseline, patients

who subsequently had a new event had higher values of ABP 24 hour 142.3 ± 17 vs 133.1 ± 14 mm Hg and also daytime 144.6 ± 19 vs 136.1 ± 14 mm Hg, nighttime 137.2 ± 19 vs 127.3 ± 16 mm Hg and 24 hour systolic variability 14.6 ± 3.vs 16 ± 4 mm Hg. No significant differences were found for metabolic parameters and for casual BP. In a Cox regression analysis only 24 hour SBP and nighttime SBP values were independent ($P < 0.05$) predictors of new total CV events after adjustment to age, BMI, diabetes, medication, casual SBP and corresponding diastolic BP. When the sample was divided by the cut off of PP< vs ≥55 mm Hg significant survival curves free of event were observed (log rank 9.01 $P < 0.003$. Concerning fatal CV events (n = 23) only 24 hour-PP and nighttime SBP were independent ($P < 0.05$) predictors of CV mortality.

Conclusions: In patients with previous CV events ABP (but not casual BP) especially high 24-hour SBP, nighttime SBP and 24-PP > 55 mm Hg are strong predictors of new arising CV events.

Keywords: Ambulatory blood pressure; Prognosis; Previous cardiovascular events

PO-305

METHODS FOR FAST AND ACCURATE NORMALIZATION OF REAL-WORLD PRESCRIPTION DATA: A REPORT FROM THE O'QUIN HYPERTENSION INITIATIVE

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Background: Research using electronic health records systems (EHRS) data requires normalization, especially across heterogeneous EHRS platforms. Prescription normalization converts data into discrete medication name, dose, and frequency fields. EHRS data often includes typographical errors, critical omissions, and extraneous insertions. Individually, the commonly used methods for automated normalization [string matching or natural language processing (NLP)] have significant limitations. Moreover, a dictionary of all prescription terms is required.

Objective: Determine if a normalization process that combines string matching and NLP will provide superior accuracy than the individual methods.

Methods: The Outpatient Quality Improvement Network (O'QUIN) Hypertension Initiative database (>700,000 hypertensive patients) was used with a custom dictionary of prescription terms. The normalization program is a series of several proven methods, optimizing each method's benefits while hindering known drawbacks.

1. Tokenization: The original text is divided into smaller strings that the following steps may manipulate independently.
2. Bias: Important words are lengthened to increase visibility. Unimportant words are shortened, e.g. "HCTZ" is replaced with "Hydrochlorothiazide" while "Hydrochloride" is replaced with "HCL."
3. String matching: In biasing, unknown words are identified. Each unknown word is compared to a dictionary of known terms using a string matching algorithm. "Vasotek" becomes "Vasotec." By only matching unknown words, time consumption and errors are limited.
4. NLP: The usage of each word is calculated. A dictionary of known usage patterns limits NLP results to well-formed patterns, avoiding ambiguity.
5. Normalization: Knowing the words and the usage of each word, the computer then identifies the medication, dosage, and frequency.

Results: String matching together with NLP provides prescription drug normalization accuracy of >95% for drug name, >90% for drug dose and ~85% for drug frequency, which exceeds the best results reported by other groups.

Conclusion: A fixed sequence of string matching and NLP with proven normalization strategies classifies prescription medications with accuracy that exceeds the best results reported by other groups. Automatic and accurate normalization of large clinical datasets for health services research is enhanced.

Keywords: Fast and accurate normalization; Prescription data

PO-305A

HIGH BLOOD PRESSURE TREATMENT AMONG BLACK AND WHITE STROKE PATIENTS

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Background: Secondary stroke prevention remains a key component of all stroke programs. In addition to stroke specific strategies, the treatment of co-morbid conditions such as hypertension is an important consideration. In addition to racial disparities in the incidence of stroke, racial disparities are also seen in the prevalence and age of onset of hypertension and diabetes. The purpose of this study was to assess racial differences in the prevalence and treatment of comorbid conditions among a stroke cohort.

Methods: One year follow up telephone survey of 384 subjects from the Stroke Education and Prevention in South Carolina Study cohort who were aged 45 years or older and discharged with a primary diagnosis of stroke (ICD 9 430–438) from October 1, 2008 to September 30, 2009.

Results: Thirty percent of the stroke patients were Black with a significantly higher proportion of strokes <65 years of age 59.5% compared to 42.4% of the White stroke patients. Among those patients with hypertension, 35.7% also had diabetes, 83.3% had dyslipidemia, and 16.2% had atrial fibrillation. Blacks had significantly higher proportions of hypertension (94.6 vs 87.4%, $P = 0.03$) and diabetes (48.7% vs 26.8%, $P < 0.0001$). Blacks were 2.7 times more likely to have both hypertension and diabetes compared to Whites ($P < 0.0001$). Hypertension was treated in 74.2% of the White hypertensives and 73.7% of the Black prior to the stroke. Treatment was initiated in 26% of the hypertensive stroke patients after the stroke (25.9% among the White hypertensives and 26.3% among the Black) with treatment changes after hospitalization among another 31.7% of the hypertensives.

Conclusion: These findings confirm the known association of hypertension and risk of stroke. Of concern is the high number of patients who had hypertension treatment initiated during or soon after their stroke hospitalization. Hypertension treatment is significantly affected by the stroke with modification in therapy in over half of the stroke patients with high blood pressure suggesting that the stroke reduces clinical inertia. However, these findings suggest that the under treatment of hypertension and the lack of hypertension control remains a significant contributing factor to stroke risk.

Keywords: Stroke; Antihypertensive therapy

Cellular Mechanisms (Cell Biology; Cell Membrane Transport/Ion Channels; Coagulation/Thrombosis; Growth Factors)

PO-306

PHARMACOLOGICAL INHIBITION OF PI3KΓ REDUCES BLOOD PRESSURE BY A VASORELAXANT AKT/LTCC MECHANISM

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Arterial hypertension is the most consistent and powerful predictor of cardiovascular events. For this reason antihypertensive treatment is of paramount importance to reduce cardiovascular risk, and being it is still an unfulfilled goal in refractory patients, the need of novel therapeutic strategies clearly emerges. In this study we demonstrate that PI3Kγ pharmacological targeting has antihypertensive effects. This effect is dependent on enhanced ex vivo vasodilation, documented by in vivo decreased peripheral vascular resistance, and ex vivo by vasorelaxing effects on murine vessels. Vasorelaxation is endothelium-independent and has to be ascribed to impaired smooth muscle Akt phosphorylation and contractile response. Molecular insights reveal that PI3Kγ inhibitors affect smooth muscle L-type calcium channel (LTCC) current density and calcium mobilization, by impairing plasma membrane translocation of α1C LTTC subunit, responsible for channel open-state probability. Overall our data show a novel way to regulate calcium fluxes through LTCC by PI3Kγ inhibition, that appears to have upcoming possibilities to be exploited as a novel tool in hypertension.

Keywords: Intracellular signaling; L-type calcium channel; PI3K gamma; Vascular contraction

PO-307

HYPERTENSION INDUCES β-AMYLOID DEPOSITION AND COGNITIVE IMPAIRMENT BY ACTIVATING RAGE IN BRAIN ENDOTHELIUM

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Hypertension has been associated to Alzheimer's Disease (AD) for a long time but the pathophysiological mechanism responsible for this association is still elusive. We have studied this association in a murine model of hypertension, showing typical traits of AD, such as β-amyloid (Aβ deposition, cognitive impairment, brain hypoperfusion and neuroinflammation.

In this work we investigate the molecular mechanisms activated by high blood pressure in brain, to induce the AD pathological changes observed in mice in which hypertension was induced by transverse aortic coarctation (TAC), selectively imposing pressure overload impact to the cerebral circulation. We found that the Receptor for Advanced Glycation End-products (RAGE), that critically regulates Aβ transport at the Blood Brain Barrier (BBB) was early activated in brain endothelium by hypertension. We therefore subjected RAGE KO and WT mice to hypertension by TAC. Strikingly, RAGE KO mice were protected by hypertension-induced AD pathological alterations. In particular we found a milder neuroinflammatory profile, in terms of microglia activation and cytokine production. Furthermore, RAGE ablation rescued the deficits in learning and memory tasks as well as Aβ deposition in brain parenchyma, induced by hypertension. Overall we show that hypertension induces RAGE activation in brain endothelium triggering the chain of brain pathological alterations typical of AD pathology.

Keywords: Cognitive decline; Brain endothelium; β-amyloid; Receptor for advanced glycation end-products

PO-308

DOWNMODULATION OF PEROXIREDOXIN-3 EXPRESSION IN CARDIAC FIBROBLASTS BY ANGIOTENSIN II

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The aim of this study was to determine whether angiotensin II (ANG II) affects the protein and mRNA expression of the mitochondrial antioxidant peroxiredoxin-3 (PRX-3) in cardiac fibroblasts through inducing the phosphorylation of the proteins Akt and FOXO3a, thereby contributing to the oxidative stress in the myocardium.

Cardiac fibroblasts (passage 2) from normal male adult rats were cultured to confluency and incubated in serum-free Dulbecco's modified Eagle's medium for 24 hours. The cells were then preincubated with/without the tested inhibitors fot 1 hour and further incubated with/without ANG II (1 μmol/L) for 24 hour.

ANG II increased ($P < 0.001$) the production of reactive oxygen species in cardiac fibroblasts from 389 ± 36 to 695 ± 66 a.u./10^6 cells (n = 10). ANG II decreased ($P < 0.01$) the mRNA and protein expression of PRX-3 by $36.9 \pm 3.0\%$ and $29.7 \pm 2.7\%$ (n = 4), respectively. The likely mechanism through which ANG II produces the effect of reducing PRX-3 expression is by reducing the extent of binding of FOXO3a to the PRX-3 promoter. In control fibroblasts inhibition of FOXO3a transcription with small-interfering RNA (siRNA) led to a reduction in PRX-3 gene expression.

Our data also shown that when Akt is phosphorylated by ANG II, P-Akt is translocated from the cytoplasm to the nucleus, subsequently nuclear phosphorylation of FOXO3a by P-Akt leads to relocalization of FOXO3a from the nucleus to the cytosol, resulting in a decrease its transcriptional activity, and consequently in PRX-3 expression. The likehood of such a mechanism is further strengthened by the fact that inhibition of phosphoinositide 3-kinase with wortmannin or LY 294002 was shown to lead to a decrease in P-Akt and to a consequent increase in PRX-3 expression.

Our data indicate that ANG II inactivates FOXO3a by activating Akt, leading to a reduction in the expression of the antioxidant PRX-3, and thereby potentially contributing to oxidative stress in the myocardium.

Keywords: Angiotensin II; Cardiac fibroblasts; Peroxiredoxin-3; Oxidative stress

Lipid Metabolism

PO-309

DOES THE ASSOCIATION BETWEEN LIPID PROFILE AND OBESITY INDICES VARY THROUGH DECADES IN ESSENTIAL HYPERTENSIVE PATIENTS?

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There is a known interaction between obesity, lipid profile and arterial hypertension. The aim of the present study was to assess the association between different patterns of obesity to lipid profile in essential hypertensive patients. Further, these possible associations were explored taking into consideration different periods of time from 1987 to 2010.

The study cohort comprised 22,000 consecutive, essential hypertensive patients who referred to our outpatient clinics from 1987 to 2010. Patients were subjected to full clinical and laboratory evaluation. Further, previous antihypertensive and hypolipidemic treatment was assessed through medical history. Study population was further divided in six groups according to the time of referral to our clinics [group I (from 1987 to 1990), group II (from 1991 to 1994), group III (from 1995 to 1998), group IV (from 1999 to 2002), group V (from 2003 to 2006) and group VI (2007–2010).

Overall, a strong positive association was observed between total cholesterol (TC), triglycerides (TGL), low-density lipoprotein (LDL), apolipoprotein B (ApoB) with all obesity markers ($P < 0.0001$) both in univariate and multivariate analysis. High density lipoprotein (HDL) and apolipoprotein A (ApoA) were negatively associated with obesity indices ($P < 0.0001$). The associations remained strongly significant ($P < 0.0001$) when comparing the six time period groups, while LDL gradually decreased from past to recent years ($P < 0.0001$) and obesity markers tent to worse nowadays ($P < 0.0001$).

In essential hypertensive patients there is a strong correlation between lipid profile and obesity markers independently of several co-factors. Assessing the differences among six periods of referral time in our clinics, it appears that when approaching recent years, patients even though more obese present with a better lipid profile.

Keywords: Lipid profile; Obesity; Arterial hypertension

Neural Hormonal Mechanisms (Renin; Neural Control; Vasoactive Autacoids)

PO-310

LONG TERM FOLLOW-UP OF PATIENTS WITH POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME

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Postural orthostatic tachycardia syndrome (POTS) is defined as the presence of orthostatic symptoms with a heart rate increment ≥30 bpm without orthostatic hypotension. POTS clinical presentation and pathophysiological mechanisms are heteregoneous and prognosis uncertain. We assessed long term follow-up (FUP) of patients (pts) with POTS who underwent tilt test (TT) in a tertiary care centre and the impact of therapeutic measures. We retrospectively analyzed clinical records of pts with orthostatic intolerance symptoms, who underwent HUT where POTS was diagnosed, from January 1997 to December 2008. Demographic and clinical data were analyzed. A FUP interview was conducted by phone focusing therapeutic measures and subjective perception of present symptoms. A total of 34 pts were included. Median age at time of TT was 24 (11–57) years; 30 (88.2%) were women. Two women had asthma, two psychiatric disorders, one type 1 diabetes mellitus, one fibromyalgia and other woman hyperthyroidism; a 26 years old man had acute myeloid leukemia (AML). Dizziness was present in 23 (67.6%); syncope in 20 (58.8%); blurred vision in 18 (52.9%); diaphoresis, palpitations and pallor in 15 (44.1%); 7 (20.6%) had headache; and 5 (14.7%) nausea. Less frequent (<10%) symptoms were asthenia, chest pain, dyspnea, tremor, vomit, heat and cold. FUP was achieved in 17. Mean FUP time was 92 ± 41 (3–144) months. All except one, deceased with AML, were alive by the time of contact. Ten (62.5%) and 8 (50%) pts increased fluid and salt intake, respectively; 11 (68.8%) used physical maneuvers and two elastic support hosiery. Fifteen (93.8%) used drug therapy in any moment during FUP. β-blockers were (BB) used in 14 (87.5%) pts, ansiolitics in 8 (50%), selective serotonin reuptake inhibitors (SSRI) in 7 (43.8%), fludrocortisone in 6 (37.5%), midodrine in 5 (31.3%). Nowadays, only 10 (62.5%) pts are under drug therapy: 8 (50%) with BB, 4 (25%) with ansiolytics and 2 (12.5%) with SSRI. Five (37.5%) pts are asymptomatic, 9 (60%) feel better and one did not improve. In the previous year 10 (62.5%) had no symptoms, but one had weekly episodes and another two daily episodes.

POTS is a heterogenous clinical entity with variable but with a benign outcome. The majority of pts symptoms improved with a comprehensive therapeutic (pharmacologic and non-pharmacologic regimen).

Keywords: Postural orthostatic syndrome; Autonomic nervous system; Prognosis

PO-311

RESISTANT HYPERTENSION AND INTRAVASCULAR VOLUME EXPANSION

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Introduction: Inadequately controlled and resistant hypertension is an enormous public health problem in the world.

Methods: This study included 168 consecutives women (without sex hormones) and men, with resistant hypertension. This group was compared with a control group of 55 normotensive individuals. Characteristics of both groups were similar (age, gender, BP, BMI,..). All patients considered to have essential hypertension. Patients were submitted to: 24 hour Blood Pressure, plasma rennin activity (PRA; normal: 7–76 μU/mL), plasma aldosterone concentration (PAC; normal:40–310 pg/mL), Urinary Aldosterone (U Aldo; normal: 2–6 μg/24 h) (PAC/PRA ratio, brain-type natriuretic peptide (BNP; normal: <100 pg/mL), plasmatic cortisol (P Corti; normal: 5–25 μg/dL), plasmatic sodium (P Na; normal:136–146 mmol/L) and potassium (P K; normal:3.5–5.1 mmol/L).

Results: The resistant hypertension subjects were older than control subjects. Twenty-four hour Arterial Blood Pressure were higher in resistant hypertensive group (149 ± 1.4/89 ± 1.1 mm Hg). In resistant hypertension subjects vs controls we

obtained lower values of PRA (4.5 ± 0.3 vs 7.5 ± 6.0 ± 0.5 μU/mL, $P < 0.05$) and P K (3.8 ± 0.1 vs 4.4 ± 0.04 mmol/L, $P < 0.001$) and higher values of PAC (342 ± 11.8 vs 190 ± 9.1 pg/mL, $P < 0.0001$), PAC/PRA ratio (28 ± 1.9 vs 8.1 ± 0.8, $P < 0.0001$), U Aldo (13.9 ± 0.5 vs 9.2 ± 0.8 μg/24 h; $P < 0.05$), P Corti (29.3 ± 3.1 vs 19.7 ± 2.9 μg/dL) and BNP (42.1 ± 4.0 vs 19.9 ± 4.2 pg/mL, $P < 0.001$). Among patients with resistant hypertension, PAC, PAC/PRA ratio, plasmatic cortisol, U Aldo and BMI were significantly higher in males when compared with females.

Conclusions: Raised levels of PAC,.PAC/PRA ratio, U Aldo, P Corti and BNP in patients with resistant hypertension are favorable to intravascular volume expansion, such occurred in primary aldosteronism. These differences are discreetly pronounced in old age patients and males subjects.

Keywords: Resistant hypertension; Plasmatic volum; Aldosterone; Renin

PO-312

EXPRESSION OF THE RENIN-ANGIOTENSIN SYSTEM IN A HUMAN PLACENTAL CELL LINE

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The renin-angiotensin system (RAS) is present in human placental tissue and appears to participate in the regulation of maternal-fetal blood flow during normal pregnancy. The activation of the uteroplacental RAS may be one of the mechanisms underlying the deficiency of uteroplacental perfusion in preeclampsia, a hypertensive disorder in pregnancy. The expression of RAS in the placental tissue is regulated by various hormones and diseased conditions. To further understand the mechanisms underlying the regulation, an in vitro system is needed to facilitate the investigation. To reach this goal, we have studied the expression of RAS in a human placental cell line. The cells were cultured in plastic plates with medium (DMEM) and 10% fetal bovine serum. Total RNAs from these cells were prepared using Trizol and RNA was reverse transcribed. The cDNAs obtained were amplified by TaqMan real-time PCR using specific primers. Specific mRNAs for angiotensinogen, renin, angiotensin converting enzyme and angiotensin receptor type I were detected in this human placental cell line by TaqMan real-time PCR analysis. The authenticity of the PCR products was confirmed by DNA sequencing. We were unable to show angiotensin receptor type II mRNA in this human placental cell line. Angiotesin II protein, the final biological active product of RAS system was detected in the culture media from the cells by radioimmunoassay. In addition, the angiotensin receptor type I protein was identified as a 41-kDa protein in the placental cell lysate by the western blot analysis using the specific antibody. The results demonstrate that all the necessary components of RAS are expressed in the human placental cells. This human placental cell line thus is a useful in vitro system to study the regulation of RAS.

Keywords: The renin-angiotensin system; Placenta

Non-Pharmacological Therapy (Alternative Medicine; Diet; Physical Activity)

PO-313

THE HARMONY STUDY: HYPERTENSION ANALYSIS OF STRESS REDUCTION USING MINDFULNESS MEDITATION AND YOGA

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Various lifestyle modifications have been identified that lower blood pressure and reduce the risk of developing CVD. The HARMONY study is designed to evaluate the efficacy of a lifestyle intervention; mindfulness based stress reduction (MBSR) to lower blood pressure in people with stage 1, unmedicated hypertension. This RCT aims to recruit 100 adults ages 20–75 years with mean daytime ambulatory BP ≥135/85 mm Hg or 24-hour ambulatory BP ≥130/80 mm Hg, with no immediate indication for medical therapy. The MBSR intervention is a standardized 8 week program. Subjects are randomly assigned to early MBSR or a wait list delayed control group. Outcomes include 24-hour ABPM before and after MBSR course completion and 24 weeks after baseline. Other measures include demographics, anthropometric measurements, and psychological questionnaires. To date, 89 subjects have been recruited. See Table I for baseline characteristics of current subjects. The study will provide preliminary evidence to support a larger RCT by evaluating feasibility and safety of MBSR as a complementary treatment for high BP and by documenting any treatment effect. In conclusion, the results of this trial will contribute to the development of a non-pharmacological treatment approach to hypertension.

Baseline information	
Baseline demographic	Result
Sample size	89
Number of men:women	37 M:52 F
Age (years)	53 ± 14
Mean 24 hour ABPM SBP	135 ± 8
Mean 24 hour ABPM DBP	82 ± 6
Mean awake 24 hour ABPM SBP	141 ± 8
Mean awake 24 hour ABPM DBP	87 ± 6
Mean office SBP	135 ± 12
Mean office DBP	86 ± 7
Overall mean waist size (cm)	90 ± 14
Mean waist size women (cm)	84 ± 16
Mean waist size men (cm)	96 ± 9
Mean total cholesterol (mmol/L)	5.4 ± 0.9
Mean LDL (mmol/L)	3.2 ± 0.8
Mean HDL (mmol/L)	1.5 ± 0.4
Mean fasting blood sugar	4.9 ± 0.5
Mean HBA1C (%)	5.7 ± 0.003
Mean serum creatinine (μmol/L)	73 ± 12.2
Mean MAU:creatinine ratio	0.6 ± 1.4

Keywords: Hypertension; Meditation; Relaxation therapy; Ambulatory blood pressure monitoring

PO-314

IMPACT OF SMOKING CESSATION ON NOCTURNAL BLOOD PRESSURE

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Background: As most people do not smoke after bedtime, the effects of smoking and smoking cessation on nocturnal BP, an independent risk factor for cardiovascular (CV) disease, is not well characterized. We assessed the effect of smoking cessation on nocturnal BP in a prospective clinical trial.

Methods: Patients who smoked at least 10 cigarettes per day were evaluated from a 6-week clinical trial involving use of varenicline in all patients accompanied by two different types of behavioral therapy. Patients underwent 24-hour BP monitoring at baseline and following 6 weeks of follow-up at which time the smoking status was assessed. Non-smokers were defined as those with 7-day point prevalence reports of no cigarettes, carbon monoxide $\leq$6 ppm and salivary cotinine $\leq$1 ng/mL.

Results: There were 50 patients (mean age, 41 $\pm$ 13 years) of whom 24 (48%) were not smoking at 6 weeks. Mean 24 hour BPs and nocturnal decline (awake-sleep) in BP at baseline were similar for the two groups. Baseline nocturnal systolic BPs were slightly lower in patients who became non-smokers (Table). At 6 weeks, patients who became non-smokers had both a greater decline in nocturnal BP compared with smokers as well as a larger "dip" (awake-sleep BP) compared with smokers.
The nocturnal decline in systolic BP for those who became non-smokers went down while in continued smokers went up (-1.1 $\pm$ 9.5 vs 3.8 $\pm$ 8.8 respectively, P = 0.07).

Conclusion: These data show that cessation of smoking is associated with a reduction in the nocturnal BP as well as a relative increase in "dipping" in normotensive smokers. These findings suggest that smoking cessation may have additional benefits by improving the circadian rhythm of BP.

Table I. Blood pressure findings for non-smokers vs smokers

Parameter	Non-Smokers, N = 26	Smokers, N = 24	P-value SBP/DBP
24-hour BP (mm Hg)			
Baseline	121/73 $\pm$ 10/6	124/73 $\pm$ 10/7	0.16/0.99
Week-6	124/75 $\pm$ 11/6	126/73 $\pm$ 12/6	0.47/0.24
Nocturnal BP			
Baseline	108/62 $\pm$ 13/8	114/64 $\pm$ 11/8	0.07/0.20
Week-6	112/64 $\pm$ 11/7	118/66 $\pm$ 15/9	0.12/0.20
Nocturnal Decline (mm Hg)			
Baseline	-15/-14 $\pm$ 7/5	-14/-11 $\pm$ 9/8	0.55/0.10
Week-6	-16/-15 $\pm$ 6/5	-11/- 9 $\pm$ 9/6	**0.009/<0.001**
Awake-sleep decline (%) in SBP at Week-6	12.7 $\pm$ 4.4	8.4 $\pm$ 7.1	**0.01**

Bold typeface for statistically significant values.

Keywords: Ambulatory blood pressure monitoring; Smoking cessation; Nocturnal blood pressure; Risk factor reduction

PO-315

LEISURE PHYSICAL ACTIVITY AND EMERGENT CARDIOVASCULAR RISK FACTORS IN HYPERTENSIVE PATIENTS

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Regular physical activity lowers the risk of cardiovascular events with a mechanism that could involve inflammatory markers. We examined the relationship between the levels of leisure physical activity and both classic and emergent cardiovascular risk factors in 321 untreated essential hypertensive patients (58 $\pm$ 11 year; 161 M/160 F). In these patients we measured anthropometric indexes and the fasting levels of blood glucose, plasma insulin and C-peptide levels, HOMA-index, the glucose and insulin response to an OGTT, plasma lipid levels, lipoprotein(a), homocysteine, fibrinogen, D-dimer, prothrombin fragment 1 + 2 (F1 + 2), PAI-1, tPA, C and S coagulation proteins, antithrombin III (ATIII), and C reactive protein (CRP). The average weekly level of leisure physical activity of the last 6 months was assessed by a questionnaire. We considered only aerobic activity and patients performing agonistic activities were excluded. The level of physical activity was classified according to the questionnaire as follows: 0, only home activities (n = 189; age 59 $\pm$ 13 year; M 91, F 98); (1) <30 minutes of activity for 3 days in a week (n = 50; age 57 $\pm$ 9 year, M 24/F 26; weekly energy consumption 732 $\pm$ 572 Kcal/w); (2) more than 30 minutes of physical activity for at least 3 days in a week (n = 82; age 56 $\pm$ 10 year; M 46/F 36; weekly energy consumption 1839 $\pm$ 1406 Kcal/w). Sedentary patients had greater body mass index, plasma insulin levels, and HOMA-index, worse glucose and insulin response to an oral glucose load, and increased plasma fibrinogen and D-dimer levels than active patients (Table). No differences were found among groups in plasma lipids, lipoprotein(a), homocysteine, PAI-1, tPA, F1 + 2, C and S coagulation proteins, ATIII, and CRP levels. Thus, in hypertensive patients moderate leisure physical activity is associated to greater sensitivity to insulin and lower prothrombotic risk, but not with changes of other inflammatory markers.

Variables	Levels of physical activity 0	1	2	P (ANOVA)
BMI (kg/m^2)	28.8 $\pm$ 4.7	28.7 $\pm$ 4.4	27.4 $\pm$ 3.2	0.045
Insulin (μU/mL)	12.8 $\pm$ 8.7	12.4 $\pm$ 8.1	10.0 $\pm$ 4.9	0.024
HOMA-index	3.36 $\pm$ 2.89	2.96 $\pm$ 2.01	2.54 $\pm$ 1.25	0.038
AUC glucose	405 $\pm$ 102	404 $\pm$ 97	372 $\pm$ 82	0.031
AUC insulin	245 $\pm$ 148	230 $\pm$ 105	170 $\pm$ 91	<0.001
Fibrinogen (mg/dL)	373 $\pm$ 96	385 $\pm$ 76	345 $\pm$ 69	0.017
Log D-dimer (μg/mL)	2.44 $\pm$ 0.24	2.41 $\pm$ 0.23	2.34 $\pm$ 0.14	0.003

Keywords: Leisure physical activity; Insulin resistance; Fibrinogen; D-Dimer

PO-316

AEROBIC EXERCISE TRAINING IMPROVES RENAL FUNCTION IN AFRICAN AMERICANS

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African Americans are disproportionately afflicted with end-stage renal disease and progress to advanced stages of kidney disease from early disease states at greater rates in comparison to other ethnic groups. As such, early preventive measures to prevent the rapid deterioration of renal function in African Americans may be of clinical importance as the national healthcare paradigm shifts from disease management to disease prevention. The purpose of this study, therefore, was to determine the effects of a 6 month aerobic exercise intervention (AEXT) on renal function in a cohort of African Americans with normal (Glomerular filtration rate: GFR > 90 mL/min/1.73 m^2) or mildly impaired renal function (GFR 60–89 mL/min/1.73 m^2). Seventeen African

Americans (52 ± 6 years) who were sedentary, non-diabetic, non-smoking, free of cardiovascular disease and not on antihypertensive medication completed 6 months of supervised AEXT (3 days/week, 65% of VO2max, 40 min/session). Before and after AEXT, 24-hour ambulatory blood pressure monitoring was conducted and fasted blood samples were collected for calculation of GFR using the MDRD equation. GFR significantly increased 7.4% from pre-exercise levels (pre: 91.1 ± 15.4 vs post: 97.8 ± 15.3 mL/min/1.73 m^2, $P < 0.01$). Seventy-six percent (n = 13) of the study population increased their GFR post-AEXT. The relative change in GFR was significantly associated with the relative change in both body weight ($r = -0.49$, $P < 0.05$) and BMI ($r = -0.57$; $P < 0.05$). Twenty-four-hour systolic (pre: 125 ± 9 vs post: 127 ± 10 mm Hg) and diastolic blood pressure (pre: 77 ± 6 vs post: 77 ± 7 mm Hg) did not significantly change after AEXT, and were not associated with changes in GFR. Sub-analysis of subjects categorized as having mildly impaired renal function (n = 9) showed that GFR was significantly increased 11.4% from pre-exercise levels (pre: 79.1 ± 8.5 vs post: 88.1 ± 9.4 mL/min/1.73 m^2, $P < 0.01$), with 33% (n = 3) of subjects no longer being categorized as having mildly impaired renal function. Our preliminary findings suggest that AEXT may improve renal function in African Americans without overt kidney disease. The mechanisms for this improvement in renal function appear to be, in part, dependent on changes in body mass and independent of the influence of blood pressure.

Keywords: Renal function; Aerobic exercise; African Americans; Ambulatory blood pressure

PO-317

ACTIONS TO CONTROL HYPERTENSION AMONG ADULTS WITH HYPERTENSION

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About 30% of US adults have hypertension. Treatment guidelines include therapeutic lifestyle modification to lower blood pressure as the initial step to be followed with antihypertensive medication if the hypertension remains uncontrolled. Using the Behavioral Risk Factor Surveillance System (BRFSS) data, 2009, we report the prevalence of taking actions to control hypertension among adults with hypertension by sociodemographic and self-reported co-morbid characteristics. BRFSS is a state-based, random-digit – dialed telephone survey of the US civilian, noninstitutionalized population aged ≥18 years. Participants were classified as hypertensive if they answered "Yes" to question "Were you told on two or more different visits to a doctor or other health professional that you had hypertension?" These respondents were then asked the following questions about actions they were currently taking to control their hypertension: "Are you changing your eating habits to help lower or control your high blood pressure?" "Are you cutting down on salt to help lower or control your high blood pressure?" "Are you reducing alcohol use to help lower or control your high blood pressure?" "Are you exercising to help lower or control your high blood pressure?" "Are you currently taking medicine for your high blood pressure?" Data were weighted to 2009 state population estimates. Prevalence estimates and 95% confidence intervals were calculated. During 2009, a total of 36,622 of 118,047 participants (22.8%, standard error (SE) 0.20) were classified as having hypertension based on their self-report. Among hypertensives, 98.1% (0.15) reported taking at least one action to control hypertension. Majority of respondents reported taking each of the five actions: 73.9% (0.42) changed their eating habits; 73.8% (0.43) decreased use of salt; 80.7% (0.38) reduced alcohol consumption; 68.7% (0.44) exercised, and 87.2% (0.41) took antihypertensive medications. Almost 36% (0.43) reported taking all five actions to control hypertension. Large disparities existed regarding the action. In generally, women, blacks, those had personal doctor and those with co-morbidity conditions, including, diabetes, high cholesterol, coronary heart disease and stroke were more likely to take action than men, non-blacks, those had no personal doctor and those without co-morbidity conditions. While majority of patients were taking some types of action to control hypertension, only 36% were taking all the recommended actions.

Keywords: Lifestyle intervention for hypertension; BRFSS

PO-318

EXERCISE CAPACITY IS INVERSELY RELATED TO MORTALITY RISK IN HYPERTENSIVE INDIVIDUALS WITH SLEEP APNEA

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Introduction: Both hypertension and sleep apnea are associated with relative high mortality risk. Increased exercise capacity is associated with lower mortality risk. The interaction between sleep apnea, mortality risk and exercise capacity has not been investigated.

Methods: From April of 1996 to June 2010, we identified 538 hypertensive individuals with sleep apnea (mean age: 62 ± 11) who underwent an exercise evaluation to rule out ischemia. All had a normal exercise response. We established three fitness categories based on the age and MET level achieved. Individuals who achieved a peak MET level within the lowest 25th percentile of their respective age group (<5 METs) comprised the Low-Fit category (n = 129). Those with a MET level between the 21st and 75th percentile (5–7 METs) comprised the Moderate-Fit category (n = 238) and those with a MET level above the 75th percentile (>7 METs), comprised the High-Fit category (n = 171).

Results: There were 315 deaths during the follow up period of 5.3 years (110 deaths per 1000-person years). Cox proportional hazard analysis, adjusted for age, BMI, cardiovascular risk factors and cardiac medications revealed a 13% lower risk for mortality for every 1-MET increase in exercise capacity. When compared to the Low-Fit category, the adjusted mortality risk 27% lower for the Moderate-Fit (hazard ratio = 0.73; CI: 0.56–0.94) and 53% lower higher in the Low-Fit (hazard ratio = 0.47; CI: 0.35–0.64).

Conclusions: Exercise capacity is inversely related to mortality in hypertensive individuals with sleep apnea. The relative risk of mortality was 13% lower for each 1-MET increase in exercise capacity and more than 50% lower in those with an exercise capacity >7 METs. This exercise capacity is achievable by most individuals and therefore has significant clinical and public health impications.

Keywords: Hypertension; Sleep apnea; Exercise capacity; Mortality

PO-319

HEART RATE RECOVERY, FITNESS AND MORTALITY RISK IN HYPERTENSIVE INDIVIDUALS

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Introduction: Impaired heart rate recovery (HRR) and low fitness are associated with higher mortality risk. In addition, HRR is influenced by fitness status. Hypertensive individuals have relatively lower exercise capacity than normotensive. The interaction between HRR, mortality and fitness in hypertensive individuals has not been defined. Thus, we sought to evaluate the association between HRR and all-cause mortality and to assess the effects of fitness on this association in hypertensive individuals.

Methods: Between August 1994 and January 2009, treadmill exercise testing was performed in 2690 hypertensive male veterans for clinical reasons at the Veterans Affairs Medical Centers Washington, DC. HRR was calculated at 1 and 2 minutes of recovery. All-cause mortality was determined over a mean 5.6 ± 3 years of follow-up period (15,078 person-years).

Results: There were 268 deaths during the follow up period (17.8 deaths per 1000-person years). Mortality risk, adjusted for age, BMI, cardiovascular risk factors and cardiac medications, was significantly and inversely associated with HRR, only at 2 minutes of recovery. A cut-off value of 14 beats/min at 2 minutes recovery was the strongest predictor of mortality for the cohort (hazard ratio = 2.6; CI: 1.8–4.0). When low fitness (lowest 33% percentile of exercise capacity) and low HRR were present, mortality risk was 4.1-fold higher (<6 METs and $\leq$14 beats/min) compared to the High-Fit+High-HRR group (>6 METs and >14 beats/min).

Conclusions: HRR at 2 minutes post-exercise is strongly and inversely associated with all-cause mortality in hypertensive individuals. Exercise capacity influences HRR-associated mortality substantially and should be considered when assessing mortality risk.

Keywords: Heart rate; Fitness; Hypertension; Mortality

PO-321

THE COST-EFFECTIVENESS OF INTERVENTIONS DESIGNED TO REDUCE SODIUM INTAKE

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Purpose: To synthesize the cost-effectiveness evidence of sodium-reduction interventions in the hope of increasing population-wide efforts to control hypertension.

Methods: We conducted a comprehensive literature review of journal articles published in English from January 2000 to May 2010. The databases PubMed, EMBASE, MEDLINE, and EconLit were used to search the literature. The key search terms were costs, cost-effectiveness, cost-utility, cost-benefit, medical expenditures, and "sodium" and "salt" paired with "reduction," "intake," and "consumption." In addition to abstracting evidence on cost-effectiveness, we abstracted evidence on cost savings and the costs of intervention implementation if cost-effectiveness evidence was not available in the publication. We also assessed the strengths and weakness based on data quality and analytic methods of these studies.

Results: From the 53 references obtained from the literature search, we identified 11 original research articles that provided relevant information on medical cost saving, implementation costs, or cost-effectiveness of interventions to reduce sodium intake. Eight (73%) of the 11 were conducted exclusively in developed countries. In all 11 studies, the interventions evaluated were population-wide programs. In general, the interventions were low in cost such as the cost ranging from \$0.04 to \$0.32 per person for awareness campaigns through mass-media outlets and government regulation on food products in low- and middle-income countries, suggesting their financial feasibilities in most countries. The results suggest that population-wide interventions are very cost-effective, e.g. only ARS\$151 per DALY (disability-adjusted life year) saved in Argentina. Typically, the studies in the US and Canada evaluated the impact of sodium reduction on savings in medical costs such as saving \$18 billion by reducing sodium intake to 2300 mg/day annually in the US.

Conclusion: The literature provided cost-effectiveness evidence that was in favor of population-wide interventions designed to reduce sodium intake. Reducing the intake of sodium through such initiatives might be one of the best buys in public health. Policy makers may consider such information in making decisions about resource allocation.

Keywords: Salt; Hypertension control; Cost-effectiveness

PO-322

SEASONAL EFFECTS OF BLOOD PRESSURE IN POSTMENOPAUSAL WOMEN

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The aim of this study was to determine whether oral vitamin D3 at daily doses of 10 or 25 μg affected seasonal blood pressure measurements.

Postmenopausal women (n = 305 recruited; mean age $\pm$ SD 63.8 ± 2.2 years) took part in a double blind placebo-controlled trial (ISRCTN20328039) to receive either 10 or 25 μg vitamin D3 or placebo daily for 12 months. The baseline visit for all women was between January and March 2009. Seven study visits were completed at bimonthly intervals with a total of 265 women attending the final visit. At each study visit, three blood pressure measurements were taken using a digital blood pressure monitor (OMRON 705 CP-II). The first measurement was discarded and the mean of the final two measurements was used for this analysis. Differences between the treatment groups were tested by repeated measures ANOVA (SPSS version 18).

Our preliminary analysis showed that the intervention had no effect on mean blood pressure measurements (Figure 1). However, overall there was a significant seasonal variation in mean systolic and diastolic blood pressure over the 12 month duration of the study ($P < 0.001$, repeated measures ANOVA). The mean reduction in systolic blood pressure from winter to summer was 6.5 mm Hg (Figure 1). Further analysis will involve mixed modelling in order to adjust for the possible confounding effects of body weight, weight change and physical activity. These data highlight the importance of taking season into account when designing studies where blood pressure is a key outcome measurement. Vitamin D does not appear to influence blood pressure and observational studies showing a link between vitamin D

status and non-bone health outcomes may be a result of other mechanisms that are affected by season.

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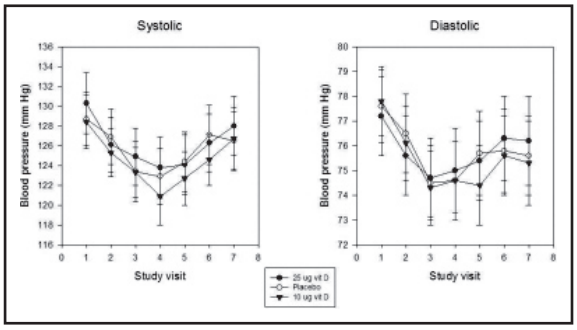

Keywords: Vitamin D; Blood pressure; Postmenopausal women; Season

Nutrition and Cardiovascular Prevention

PO-323

ANTIHYPERTENSIVE EFFECT OF DIETARY INTEGRATION WITH GRANA PADANO CHEESE IN HYPERTENSIVE PATIENTS

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The degradation of cow-milk proteins by proteinases from *L. helveticus* produces peptides with ACE-inhibitory activity and antihypertensive effect in SH rats. Two tripeptides, valyl-prolyl-proline and isoleucyl-prolyl-proline has been identified as the bioactive peptides responsible for this effect (Nakamura et al., 1995).

The Grana Padano, a typical Italian cheese, at moderate ripening degree (9–12 months), shows a potent (as measured by the spectrophotometric assay) in-vitro ACE-inhibitory effect (Magnano San Lio et al, 2009).

Aim of this study was to evaluate whether a dietary integration with a small amount of Grana Padano cheese was effective in reducing blood pressure (BP) in hypertensive patients.

In a randomized, open-label, controlled study, 45 patients received a daily dose of 30 g of 9 month-aged Grana Padano cheese for a period of 2 months. BP was evaluated before and after treatment by using conventional sphygmomanometry (average of 3 readings), automated office BP (AOBP, BpTRU M D, Canada) and ambulatory BP measurement (ABP). The results have been compared with those obtained in a control group of 15 hypertensive patients. Pharmacological and non-pharmacological treatments were stable during the previous 3 months and along the entire observation period and excluded ACE-inhibitors and Angio-2-receptor blockers. A dietary manipulation was performed in order to maintain unchanged calorie, cholesterol and sodium intake.

Preliminary results indicate that the patients who received Grana Padano cheese presented a statistically significant decrease in systolic and diastolic BP (Student's *t* test). No change in BP was detected in the control group.

In conclusion, a moderate intake of Grana Padano cheese seems to be effective in lowering BP in hypertensive patients. Appropriate (and easily feasible) dietary manipulations can counterbalance the increased intake in cholesterol and sodium due to dietary integration by Grana Padano cheese.

Table I. Change in daytime ABP values (mm Hg ± SD)

	Baseline	After treatment	*P* value
Daytime ABP in treated patients	146/91 ± 11/9	134/83 ± 10/7	<0.05
Daytime ABP control group	149/93 ± 13/8	147/91 ± 12/10	NS

No change in serum LDL-cholesterol, Calcium levels and urinary sodium excretion were observed.

Keywords: Milk-derived bioactive peptides; Grana Padano cheese; Hypertension; ACE-inhibition

PO-324

ABNORMAL CIRCADIAN BLOOD PRESSURE VARIABILITY IN HEALTHY ADULTS: A FUNCTION OF WEIGHT GAIN, INCREASE IN WAIST CIRCUMFERENCE AND INSULIN RESISTANCE

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Background: We have shown that healthy overweight and obese adults with exacerbated systemic inflammation (sIF) and insulin resistance (IR) display abnormal circadian blood pressure variability (abn CBPV) and endothelial dysfunction (ED), both functional correlates of latent CVD risk.

Hypothesis: Weight gain in healthy adults increases adipose tissue cell size, results in sIF, IR and increases CVD risk. Abnormal CBPV is a functional measure of this risk.

Methods: Eleven healthy, normal to overweight, men (8) and women (3) had initial anthropometric, laboratory and 7-day automatic ambulatory blood pressure monitoring (7-day ABPM) measures. Repeat measures were obtained 8 week post-caloric excess (140% weight maintenance energy requirement) and 12 week post routine diet.

Results: Participants exhibited weight gain and increased waist circumference (WC) (both $P < 0.0001$). Fat cell size doubled from 0.47 (0.2) to 1.07 (0.1) ρL ($P < 0.05$) with significant IR (increased fasting serum glucose, fasting insulin and HOMA; all $P < 0.05$). With each subject serving as his/her own control and an unchanged resting clinic blood pressure; nine out of 11 (9/11) participants demonstrated significant increases in the overall mean BP and HR with 7-day ABPM. The two participants without this change demonstrated no change in insulin sensitivity. Significant increases in overall mean 7-day SBP (5/9), DBP (3/9), PP (5/9) and HR (4/9) at 8 weeks persisted at 3 months in the same nine individuals SBP (4/9), DBP (4/9), PP (3/9) and HR (3/9).

Conclusion: This is the first prospective demonstration of the link between increased WC, IR and abn CBPV in healthy human adults. Participants incurring IR demonstrated functional correlates for enhanced CVD risk.

Keywords: Waist circumference; Fat cell size; HOMA; Abnormal circadian blood pressure variability

PO-325

ENDOTHELIAL DYSFUNCTION IN HEALTHY ADULTS: A FUNCTION OF WEIGHT GAIN, INCREASE IN WAIST CIRCUMFERENCE AND INSULIN RESISTANCE

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Background: Cardiovascular disease (CVD) risk is enhanced with the expansion of visceral adipose tissue compartment, in a large measure due to increased systemic inflammation (sIF) and insulin resistance (IR). We have shown that healthy overweight and obese adults with exacerbated sIF and IR (prediabetes) display abnormal circadian blood pressure variability (abn CBPV) and endothelial dysfunction (ED), both functional correlates of latent CVD risk.

Hypothesis: Weight gain in healthy adults results in IR and increases CVD risk. Endothelial dysfunction, an initial step in the process of atherosclerosis, is a functional measure of this risk.

Methods: Initial, 8 week post-caloric excess (140% weight maintenance energy requirement) and 12 week post (routine diet) anthropometric, laboratory measures were obtained in eleven healthy, normal to overweight, men (8) and women (3). Nine subjects had endothelial function (EF) reported as relative hyperemia index (RHI): increased test finger peripheral arterial tone (PAT) relative to control (endoPAT: Itamar Medical).

Results: Participants gained weight [7.2 (0.8) kg], [mean (SEM); $P = 0.0001$], increased waist circumference (WC) [8.4 (1.2) cm; $P < 0.0001$] and displayed significant IR [fasting serum glucose +8.1 (2.9) mg/dL; $P < 0.02$, fasting insulin +6.5 (2.2) μIU/mL; $P < 0.02$ and HOMA +0.12 (0.05); $P < 0.04$]. RHI declined ($P < 0.01$) by 0.32 (0.10) from initial 2.24 (0.13) to 1.92 (0.16) indicating ED (impaired flow-mediated PAT). This persisted 3 months post (mean decline −0.28 (0.12); $P < 0.03$).

Conclusion: This is the first prospective demonstration of the link between visceral adiposity, insulin resistance and endothelial function in healthy human adults. Eight weeks of controlled caloric excess caused weight gain, increased WC and IR in healthy adults. This was also accompanied by persistent (3 months post) abnormal functional correlates indicating enhanced CVD risk.

Keywords: Endothelial dysfunction; HOMA; Waist circumference; Caloric excess

PO-326

RELATIONSHIP BETWEEN SALT INTAKE AND CENTRAL AORTIC HEMODYNAMICS IN A COHORT OF UNTREATED HYPERTENSIVE PATIENTS

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Central pulse pressure (PPc) predicts cardiovascular (CV) outcomes. High salt intake has been related with blood pressure (BP) rise as well as with increased CV risk particularly with stroke. The aim of the present study was to examine in untreated hypertensive subjects the relationship between salt intake and central aortic hemodynamics and PPc (radial and carotid applanation tonometry, Sphygmocor) and pulse wave velocity (PWV, Complior). We evaluated 232 untreated nondiabetic hypertensive patients (64% female) ageing 51 + 13 years, BMI 29 ± 5 kg/m^2, PWV 11.1 ± 2.3 m/s, office pulse pressure (PPo) 64 + 17 mm Hg, 24 hour pulse pressure (PP24h) 53 + 10 mm Hg, nighttime systolic BP fall 9.4 + 6.9%, central pulse pressure (cPP) 48 ± 10 mm Hg, mean central arterial (MAPc) 101 ± 16 mm Hg central augmentation pressure (Aug P) 144 ± 29 mm Hg and central augmentation index (AIx) 27.6 ± 15.6%, 24 hour urinary (controlled for creatinuria) sodium excretion (UNa+) 202 ± 71 mmol/day and potassium (Uk+) 49 ± 16 mmol/day. After adjustment for age, BMI, gender, smoking, PWV and MAPc, the 24 hour urinary sodium excretion (but not urinary Na/K+ ratio) was independently associated with central PP ($P < 0.02$) and 24 hour PP and central AIx (both $P < 0.05$). In conclusion our data suggest that in these untreated hypertensive patients high salt intake is associated with abnormal central hemodynamic and increased central BP independently of peripheral BP. It is plausible that by these effects high salt intake may aggravate CV prognosis whereas reduction in salt intake is prone to improve central pressures and CV prognosis.

Keywords: Salt intake; Central blood pressure; Pulse wave velocity; Hemodynamics

PO-327

EFFECT OF LIFESTYLE MODIFICATION IN MENOPAUSAL WOMEN WITH OBESITY, HYPERTENSION, AUTONOMIC AND ENDOTHELIAL DYSFUNCTION

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Objectives: To identify the effect of a hypocaloric diet and aerobic physical exercise on cardiovascular risk factors of obese women in fertile age and after menopause.

Methods: Sixty-one obese people were divided in four groups, Group1:(G1) nine men (mean age 34.8 ± 7.0), Group2: (G2) 18 menopausal women (mean age 52.9 ± 5.8), Group3: (G3) 10 fertile women without contraception pills (mean age 33.3 ± 6.8) and Group4:(G4) 24 fertile contraceptive users women (mean age 32.8 ± 6.9). We evaluated: anthropometric parameters; hemodynamic, with non-invasive arterial pressure wave (Finapress), autonomic nervous system, spectral analysis of RR interval and SB variability were calculated by Fast Fourrier Transform. Baroreceptor spontaneous gain obtained by the correlation between LF bands (αindex). This evaluation was performed before and after (1 year) the implementation of Mediterranean diet and prescription of aerobic physical exercise.

Results: Means difference between first and last evaluation Δ. ΔWeight (kg) G1:-5.4 ± 1.5 ($P < 0.00$), G2:-6.3 ± 5.0 ($P < 0.00$), G3:-6.3 ± 3.7 ($P < 0.00$), G4:-6.1 ± 3.0 ($P < 0.00$); ΔBMI (kg/m^2) G1:-1.6 ± 0.7 ($P < 0.00$), G2:-2.5 ± 2.0 ($P < 0.00$), G3:-2.6 ± 1.4 ($P < 0.00$), G4:-2.4 ± 1.2 ($P < 0.00$); ΔWC (cm) G1:-4.6 ± 2.8 ($P < 0.00$), G2:5.2 ± 4.3 ($P < 0.00$), G3:-5.2 ± 2.8 ($P < 0.00$), G4:-7.1 ± 5.5 ($P < 0.00$); ΔSBP (mm Hg) G1:-16.2 ± 18.9 ($P < 0.03$), G2:-19.7 ± 11.4 ($P < 0.00$), G3:-14.1 ± 12.1 ($P < 0.00$), G4:-15.9 ± 12.5 ($P < 0.00$); ΔDBP (mm Hg) G1: -13.6 ± 11.8 ($P < 0.00$), G2:

-15.2 ± 11.7 ($P<$), G3:12.8 ± 12.2 ($P < 0.00$), G4: -12.6 ± 11.1 ($P < 0.00$); ΔHR (bpm) G1:-5.7 ± 10.8 ($P<$), G2:-7.3 ± 7.9 ($P < 0.00$), G3:-10.5 ± 8.5 ($P < 0.00$), G4:-5.3 ± 6.7 ($P < 0.00$); ΔHF_RR (ms/mm Hg) G1:440.7 ± 32.4 (ns), G2:-300.1 ± 17.7 ($P < 0.05$), G3:-40.3 ± 27.5 (ns), G4:-78.5 ± 20.7 (ns); ΔLF_SBP (mm Hg 2) G1:-2.1 ± 0.7 ($P < 0.02$), G2: -1.6 ± 0.5 ($P < 0.00$), G3:-2.3 ± 0.8 ($P < 0.01$), G4 -1.6 ± 0.4 ($P < 0.00$); ΔBR_td (ms/mm Hg) G1: 1.43 ± 1.0 (ns), G2:3.3 ± 0.7 ($P < 0.00$), G3:2.5 ± 0.5 ($P < 0.00$), G4:4.2 ± 0.6 ($P < 0.00$, ΔAdrenaline (pg/mL) G1:-1.6 ± 1.0, G2:-3.8 ± 2.2 (ns), G3:-7.7 ± 4.1 (ns), G4:-5.6Δ3.6 (ns); ΔIl-6 (ng/mL) G1:-4.8 ± 3.9 ($P < 0.00$), G2:-5.9 ± 4.0 ($P < 0.00$), G3:-5.8 ± 2.6 ($P < 0.00$), G4:-3.3 ± 2.9 ($P < 0.00$).

Conclusions: The implementation of a Mediterranean type diet with aerobic physical exercise presented benefits in all groups studied. We must highlight the improvement of autonomic and endothelial dysfunction in menopausal women.

Keywords: Obesity; Hypertension; Autonomic nervous system; Menopause

PO-328

AT RISK OLDER LATINO MEN AND WOMEN: BLOOD PRESSURE, BODY MASS INDEX AND DASH ACCORDANCE

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Purpose: Little is known about hypertension-associated risk factors among older Latinos, including dietary patterns such as DASH (Dietary Approaches to Stop Hypertension). Therefore, the purpose of this study was to identify differences in older Latinos' scores on the DASH eating plan and body mass index (BMI) by blood pressure (BP) status (normotensive, prehypertensive and hypertensive).

Methods: Older Latinos (>50 years) were recruited from health fairs, community centers, senior centers, and word of mouth in predominantly Latino Chicago communities. BP was measured in triplicate by Omron IntlliSense™ and categorized according to JNC7. BMI was calculated as weight (kg)/height^2 (m). DASH scores were calculated according to Mellen et al. (2008) on the basis of responses to the Chicago Health and Aging Project food frequency questionnaire. Data were analyzed using descriptive statistics and ANOVAs with Bonferrroni post-hoc tests. DASH scores were compared across BP status with age adjustment.

Results: Of the 96 participants, the majority were older (64 ± 8.6) female (68%), overweight (BMI 30 ± 4.4), and preferred speaking in Spanish (85%). Twenty-seven percent were normotensive, 40% were prehypertensive, and 23% were hypertensive. Age-adjusted DASH scores (inclusive of supplement contribution) differed significantly across BP status ($P = 0.04$). DASH scores were significantly higher (better) for normotensives (4.7 ± 1.3) than for prehypertensives (3.8 ± 1.8) or hypertensives (3.9 ± 1.6) (score ≥4.5 is considered DASH accordant). These DASH scores are in line with national age-adjusted scores for Mexican Americans (3.2 ± 0.2) regardless of BP status. BMI did not differ according to BP status ($P = 0.34$).

Conclusion: These differences suggest that older, traditionally Latino men and women at prehypertensive and hypertensive levels should be targeted for lifestyle change interventions, especially with respect to the DASH eating plan.

Keywords: Blood pressure status; DASH; Latino; Dietary pattern

PO-329

MEDICAL AVATAR CAN SELECT PATIENTS WITH CARDIOVASCULAR RISK FACTORS

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Efficient screening for high risk population may reduce the burden of premature deaths due to cardiovascular diseases (CVD). The aim of our study was to evaluate an interactive computer-based technology to perform a mass screening for CVD risk in working population at age 39–55 years.

An intuitive interactive software based on advance video attribute terminal technology (Avatar) was developed containing virtual animated humanoid with integrated voice synthesizer communicating with touch screen panel. Data were stored in central database and estimate of CVD risk was presented to a subject.

A total of non-selected 540 subjects, with unknown CVD risk, were screened during mandatory check-up of active workers (characteristics – Table I) and 207 (38%) subjects were overweight and 99 (18%) – obese, 174 (32%) were current smokers. Hypertension was reported in 152 (28%), hypercholesterolemia (TC > 190 mg/dL) was found in 290 (54%), and hyperglycemia (FPG > 100 mg/dL) in 102 (19%) studied subjects. High CVD risk profile represented: 21 (3.8%) patients with diabetes mellitus, 20 (3.7%) with heart failure, and 11 (2%) with self-reported coronary artery disease; moreover 3 (0.6%) revealed history of myocardial infarction and 2 (0.4%) of stroke. Additionally, elevated BP was found in 57 (10%) subjects and among subpopulation of patients with self-reported hypertension, 127 (84%) were on antihypertensive drugs, and suboptimal BP control was observed in 29 (19%) analyzed workers.

CVD correctable risk factors are highly prevalent in the population of active workers including subpopulation with diagnosed hypertension. Measured risk factors profile was similar to results of previous epidemiological surveys in Poland. Results show the efficacy of new Avatar screening tool in active, potentially healthy population, facilitating selection of patients with elevated CVD risk.

Table I. Characteristics of screened population (data presented as mean ± SD)

	Active workers (n = 540)	Non-hypertensive (n = 388)	Hypertensive (n = 152)	Hypertensive vs non-hypertensive
Women/men	383/157	278/110	105/47	
Age (years)	46.7 ± 9.8	44.1 ± 9.1	53.1 ± 4.0	$P < 0.001$
BMI (kg/m^2)	26.3 ± 4.4	25.4 ± 4.0	28.4 ± 4.6	$P < 0.001$
SBP (mm Hg)	123 ± 16	119 ± 15	130 ± 15	$P < 0.001$
DBP (mm Hg)	74 ± 16	73 ± 14	75 ± 21	$P = 0.38$
TC (mg/dL)	199 ± 38	196 ± 36	204 ± 43	$P = 0.05$
FPG (mg/dL)	92 ± 16	90 ± 14	96 ± 18	$P < 0.001$

Keywords: Cardiovascular risk factors; Advanced video attribute terminal assembler and recreator; Prevention

PO-330

AEROBIC EXERCISE TRAINING IMPROVES ENDOTHELIAL FUNCTION IN PRE-HYPERTENSIVE AFRICAN AMERICANS

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Endothelial dysfunction is implicated in the etiology of hypertension. A commonly used marker of systemic inflammation, C-reactive protein, has a direct pro-atherogenic effect on the vasculature. CRP is reported to increase expression of VCAM-1 and decrease endothelial NOS. Exercise performed on a regular basis is supportive of vascular health.

The aim of this study was to investigate the effects of moderate intensity aerobic exercise on endothelial function in a population of pre-hypertensive African Americans (AA).

Nineteen pre-hypertensive AA (SBP 122 ± 11, DBP 77 ± 6; 52 ± 6 years of age) were included. All subjects were sedentary, non-smokers, non-diabetic, free of cardiovascular, lung and kidney diseases, and were not taking any medications. Blood samples were obtained following a 12-hour fast before and after 6 months of aerobic exercise training. Complete blood count, lipid panel and CRP was quantified by Quest Diagnostics Inc. Plasma NO, VCAM-1, and SOD were quantified by commercially available kits. Sub-maximal (75–80% of heart rate reserve) graded exercise treadmill tests utilizing a modified Bruce protocol were performed to assess VO2max prior to and following the exercise training period. VO2max was estimated using regression analysis. Data was analyzed by paired *T*-tests and repeated measures ANOVA (PASW Statistics 18).

The mean VO2max of the participants prior to the exercise intervention was 25.61 ± 4 mL/kg/min and improved to 28.89 ± 6 mL/kg/min, a 13% improvement ($P = 0.001$). CRP was decreased following exercise although not statistically significant. NO and VCAM-1, endothelial markers influenced by CRP were significantly ($P \leq 0.01$) altered to favor vascular health.

In a group of pre-hypertensive AA's, we observed a significant improvement in endothelial function and aerobic capacity following a 6 month exercise intervention. These results suggest that an exercise may be an appropriate means to improve endothelial function in an a population at risk for developing Stage-1 hypertension and other cardiovascular diseases.

Keywords: Hypertension; Exercise; Endothelial dysfunction

Obesity

PO-331

THE EFFECT OF BMI ON THE SYSTEMIC CATECHOLAMINE AND HAEMODYNAMIC RESPONSE TO INCREASED SYMPATHETIC ACTIVITY IN YOUNG ADULTS: A PILOT STUDY

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Obesity is associated with an increased risk of cardiovascular disease. The mechanisms underlying this relationship are not well described. Suggested factors include increased inflammation, insulin resistance and excess sympathetic nervous system activation. We characterised the haemodynamic and catecholaemine response to forearm isometric contraction (FIC) in six normal and six over-weight young adults. Twelve healthy volunteers (six female), performed isometric forearm contraction at rest and at 40% of maximum grip for 5 minutes. Plasma catecholamines were measured at baseline and after effort. Haemodynamics were recorded at 60 second intervals by a non-invasive, oscillatory, arm-cuff (Omron). Peripheral alpha and beta adrenoreceptor sensitivity and baroreceptor sensitivity were calculated by measuring haemodynamnic response to infused isophrenaline (β-agonist, 0–2 mg) and phenylephirine (α-agonist, 0–200 mg).

Baseline catecholamine concentrations were similar between the groups. Plasma norepinephrine increased to a greater extend in the over-weight group following FIC, $P < 0.0001$. Post-FIC plasma norepinephrine concentration correlated with BMI, $P < 0.01$. There was no difference in plasma epinephrine concentration post-FIC between the groups. Mean arterial pressure (MAP) was greater in the high BMI group, $P = 0.03$. Baseline MAP also correlated with BMI, $P < 0.01$, but not with the % increase in MAP post-FIC. The increase in MAP during FIC was slightly greater in the high BMI group, $16 \pm 7.0\%$ vs $12 \pm 3\%$, NS.

The greater increase in plasma norepinephrine, but not in plasma epinephrine, following FIC suggests an exaggerated sympathetic response in the high BMI group. This is further supported by the correlation between baseline MAP and BMI. Further, larger, studies are now planned to investigate this apparent association between BMI and increased sympathetic activity.

Table I. Baseline Characteristics

	Normal weight group	Over-weight group
Age (years)	26 ± 3	30 ± 3
Weight (kg)	69.8 ± 11	92.9 ± 20*
Height (m)	1.75 ± 0.10	1.71 ± 0.1
BMI (kg/m^2)	22.6 ± 1.8	31.7 ± 7.0*
Waist (cm)	77.5 ± 14	100 ± 15*
Hip (cm)	91 ± 5	111 ± 11*
Baseline MAP (mm Hg)	75 ± 9	86 ± 7*
Baseline HR (beats/min)	60 ± 10	64 ± 7

Baseline characteristics: BMI, body mass index; MAP, mean arterial pressure; HR, heart rate. Data are means ± standard deviation. (*) Different from normal BMI group, $P < 0.05$.

Keywords: Sympathetic nervous system; Obesity

PO-332

ALDOSTERONE RELEASE IS POSITIVELY CORRELATED WITH INCREASING BODY WEIGHT IN PATIENTS WITH RESISTANT HYPERTENSION

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Background: Recent studies indicate that aldosterone excess is common in hypertensive patients, particularly in patients with resistant hypertension. The etiology of this heightened aldosterone release remains obscure. Observational studies in cohorts of general hypertensive patients suggest a possible relation between aldosterone levels and obesity. The relation between aldosterone levels and body weight in patients with resistant hypertension has not been previously reported.

Objective: To determine if BMI is positively correlated with PAC, PRA, PAC/PRA and 24-hour urinary aldosterone in European-American and African-American patients with resistant hypertension (RHTN).

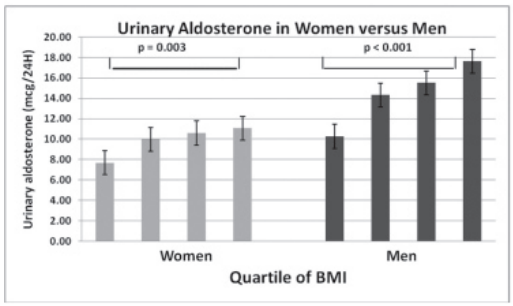
Methods: In a retrospective analysis, we examined a single-center cohort consisting of 1107 resistant hypertensive patients (60% European American, 51% men) who had been seen in a referral

hypertension clinic over a 10 year period. The relation between plasma aldosterone concentration (PAC), plasma renin activity (PRA), PAC/PRA ratio, and 24-hour urinary aldosterone (UAldo) and of body mass index (BMI) were investigated both by gender and race.

Results: Urinary aldosterone excretion was positively correlated with quartiles of BMI in men and women in a large cohort of patients with RHTN ($P < 0.001$). PAC, PRA and PAC/PRA ratio were not significantly related to BMI ($P < 0.3$). Urinary aldosterone excretion was positively related to BMI for both men and women, however, the relation was much stronger for men (Figure 1). This gender difference was also true for African American men and women.

Conclusion: In both African American and European American patients with resistant hypertension, aldosterone release was positively related to increasing BMI. The correlation was significantly greater in men. These results suggest that adiposity, particularly central adiposity more characteristic of men, contributes to excess aldosterone in patients with resistant hypertension.

Figure 1. The bar graph shows a stepwise increase of UAldo with increasing quartiles of BMI in both men and women, with the relation being stronger in men. The P value indicates that the difference of UAldo between the lowest and highest quartile.



Keywords: Aldosterone; Obesity; Resistant hypertension; Gender

PO-333

BLOOD PRESSURE IN A YOUNG, ASYMPTOMATIC, AND PHYSICALLY ACTIVE POPULATION WITH A NORMAL BODY MASS INDEX (BMI)

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Background: Obesity is a growing epidemic with significant morbidity and mortality. While BMI is but a crude surrogate marker of body fat, it remains a simple and inexpensive technique to quantify obesity. In a young, asymptomatic, and active population, we aim to determine the association of BMI with systolic (SBP) and diastolic blood pressure (DBP).

Methods: We studied 3026 subjects referred for routine employment health screening. Patients with pre-existing diabetes mellitus and/or vascular disease were excluded. Anthropometric and blood pressure measurements using a standard sphygmomanometer were taken for all.

Results: The mean age was 38.9 ± 5.4 years, 89.9% were males. The prevalence of newly-diagnosed diabetes was 2.4%. The majority of subjects were low risk using the Framingham Risk Score and ethnicity-specific Singapore Risk Score (84.5% vs 90.7%). The mean BMI was 25.2 ± 4.0 kg/m^2. Figure 1 shows a strong positive correlation between BMI and both SBP and DBP ($P < 0.001$ for both). SBP and DBP both increase significantly beyond a BMI of 22 kg/m^2 in a dose-response manner. Table I shows a general increase in the proportion of hypertensive patients with increasing BMIs beyond 20 kg/m^2 ($P < 0.001$). Patients with BMI > 20 kg/m^2 have increased odds of pre- and hypertension (OR 4.19, 95%CI 3.14–5.59).

Conclusions: Although mean blood pressures remain normal at the Asian BMI cut-off of <23 kg/m^2, the step-wise rise and additive nature of blood pressure and its consistent correlation with a rising BMI of above 20 kg/m^2 suggest that an ideal BMI conferring optimal blood pressure levels may perhaps be a below-average value of 18–22 kg/m^2 for our population (Figure 1).

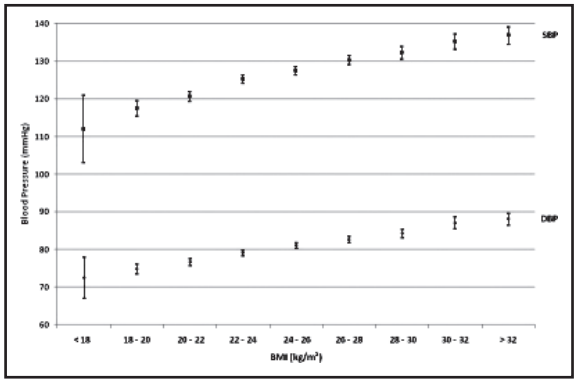

Table I. Association of BMI and prevalence of hypertension

BMI (kg/m^2)	<18	18–20	20–22	22–24	24–26	26–28	28–30	30–32	>32
Normal (%)	51.1	50.6	42.0	26.4	18.9	11.0	10.2	8.2	5.2
Prehypertension (%)	36.2	41.8	46.9	57.0	57.8	60.0	52.9	45.4	42.9
Stage 1 hypertension (%)	10.6	7.0	10.8	13.3	19.0	24.6	27.2	32.8	35.1
Stage 2 hypertension (%)	2.1	0.6	0.3	3.4	4.3	4.5	9.6	13.7	16.9

Keywords: Obesity; Body mass index; Blood pressure

PO-334

B2-ADRENOCEPTOR POLYMORPHISMS (ARG16GLY) ACCOMPANYING HIGH PLASMA NOREPINEPHRINE IS RELATED TO CARDIOVASCULAR AND RENAL COMPLICATIONS IN OBESE SUBJECTS

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Background: Obesity is known as an independent risk factor for cardiovascular and renal complications. Sympathetic nervous activation may play an important role in the onset and development of obesity and obesity-related complications. We previously reported that the Arg16Gly, β2-adrenoceptor (ADRB2) polymorphism, accompanying high plasma norepinephrine (NE) correlated to left ventricular hypertrophy (LVH) and could predict future renal injury. The 1st line of treatment for obesity is weight loss (WL). In this study, we evaluated the relationships between ADRB2 polymorphisms (Arg16Gly), plasma NE, LVH and renal function (creatinine clearance) over 2 years with WL program.

Methods: Overweight/obese Japanese men (n = 154) were measured BMI, body fat-mass, BP, plasma NE, leptin, creatinine, creatinine clearance (CCr), and ADRB2 polymorphisms (Arg16-Gly, Gln27Glu) before and after WL program (low caloric diet + exercise). Significant WL was defined >10% WL of entry BMI. LVH was determined by ECG.

Results: Significant WL was noted in 97 (63%) subjects and the frequencies of Gly16 were 44% for WL group vs 54% for non-WL group ($P < 0.05$). Subjects with Gly16 allele had higher levels of plasma NE, leptin, fat-mass, and creatinine at entry, higher prevalence of LVH, and lower CCr compared to those without Gly16 allele. WL group had lower fat-mass, plasma NE, leptin and creatinine and LVH prevalence at entry compared to non-WL group. WL group had greater absolute changes in BMI, fat-mass, Crn, CCr, plasma NE and leptin over a 2-year period. Fat-mass and plasma NE at entry correlated with Crn at both periods of entry and 12 months. Fat-mass and plasma NE at entry negatively correlated with changes in Crn over a 12-month period. CCr increased with WL and changes in CCr correlated with changes in fat-mass. In multiple regression analyses, plasma NE and fat-mass at entry and changes in NE were significant determinants for Crn at 12 months.

Conclusions: ADRB2 polymorphisms (Arg16Gly) accompanying high plasma NE is related to the prevalence of LVH and improvement of CCr during WL, demonstrating that Arg16Gly associated with sympathetic nervous activation may play an important role in cardio- and renal-complications in obesity.

Keywords: Obesity; Weight loss; Renal complications; Cardiac complications

PO-335

EFFICACY OF AN AMLODIPINE/OLMESARTAN MEDOXOMIL ALGORITHM ON BP CONTROL IN OBESE PATIENTS UNCONTROLLED BY MONOTHERAPY

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A prespecified subgroup analysis of obese patients (BMI $\geq$ 30 kg/m^2) in a prospective, open-label dose-titration study was conducted to assess the efficacy of an amlodipine/olmesartan medoxomil (AML/OM) regimen in patients (pts) who were uncontrolled on monotherapy (SBP $\geq$ 140 mm Hg [$\geq$130 mm Hg for pts with diabetes] and $\leq$180 mm Hg and DBP $\leq$110 mm Hg). Without a washout, pts were started on AML/OM 5/20 mg and up-titrated every 4 weeks for 20 weeks to AML/OM 5/40 mg, AML/OM 10/40 mg (to achieve seated (Se) BP <120/70 mm Hg), AML/OM 10/40 + hydrochlorothiazide (HCTZ) 12.5 mg and AML/OM 10/40 + HCTZ 25 mg (to achieve SeBP <125/75 mm Hg). The primary efficacy endpoint was the percentage of pts cumulatively achieving SeSBP goal <140 mm Hg (<130 mm Hg if diabetes) after 12 weeks of treatment. Of 999 pts, 505 were obese (50.6%) and mean age ($\pm$SD) was 53.3 $\pm$ 11.2 years, mean BMI was 35.8 $\pm$ 5.2 kg/m^2 and mean baseline BP was 153.1 $\pm$ 9.3/93.2 $\pm$ 8.6 mm Hg. The primary endpoint was achieved by 71.6% of obese pts. Other cumulative and noncumulative goals are shown in Table. Mean changes ($\pm$SE) from baseline BP during the titration periods ranged from -12.9 $\pm$ 0.6/-6.9 $\pm$ 0.3 mm Hg for AML/OM 5/20 mg to -25.3 $\pm$ 0.8/-14.2 $\pm$ 0.5 mm Hg for AML/OM 10/40 + HCTZ 25 mg (all $P < 0.0001$ vs baseline). At Week 20, a cumulative BP goal <140/90 mm Hg was achieved by 81.2% of pts. An ABPM substudy demonstrated that BP reductions were maintained throughout the 24-hour dosing interval in obese pts. Treatment emergent adverse events (TEAEs) occurred in 272/505 (53.9%) and drug-related (DR) TEAEs in 132/505 (26.1%) pts. The majority of TEAEs were mild-to-moderate in severity. This well-tolerated, stepped-care treatment algorithm allowed a large percentage of obese patients with hypertension uncontrolled on monotherapy to safely achieve BP control by Week 12 and 20 on an amlodipine/olmesartan-based regimen.

Table I.

Goal achievement	Cumulative[a] week 12 (%)	Noncumulative[b] week 12 (LOCF) (%)
SeSBP (<140 mm Hg; <130 mm Hg diabetes)	71.6[c]	60.6
SeBP (<140/90 mm Hg; <130/80 mm Hg diabetes)	64.8	53.2
Goal achievement	Cumulative week 20 (%)	Noncumulative week 20 (LOCF) (%)
SeBP (<140/90 mm Hg; <130/80 mm Hg diabetes)	81.2	68.8

[a]At any time point; [b]At visit; [c]Primary endpoint. LOCF, Last observation carried forward.

Keywords: Obesity; Olmesartan medoxomil; Amlodipine; BP control.

PO-336

RESOLUTION OF HYPERTENSION AFTER ADJUSTABLE GASTRIC BANDING – 1 YEAR INTERIM RESULTS OF THE LAP-BAND AP® EXPERIENCE (APEX) STUDY

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Bariatric surgery has been established as an effective treatment to reduce weight in severely obese patients refractory to behavioral and medical therapies. The objective of this study is to report the 1 year resolution and/or improvement (elimination and/or reduction in anti-hypertensive medication) of hypertension (HTN) after surgical placement of an adjustable gastric band (AGB) (AP Band, Allergan) and the accompanying change in BMI and other co-morbidities. The APEX study is an ongoing 5-year, prospective, multi-center, observational study which will assess weight reduction, co-morbidities and quality of life (QOL) after implantation of the AGB, a restrictive weight loss device. This is an interim analysis of subjects who reported daily medical therapy for HTN before AGB and who have completed the 1 year post-operative scheduled visit. At baseline, 220/436 subjects (50%) reported HTN requiring daily medical therapy, with data from 124 containing sufficient information to assess 48 week outcomes. Resolution of HTN was reported in 26 patients (21%), improvement in 72 (58%), and no change in 26 (21%). HTN did not worsen in any patient. Overall, 79% had resolution and/or improvement in HTN. Baseline BMI was not significantly different among the three groups. Mean absolute BMI change and % change in weight was -7.7/-18%, -8.0/-18.1%, and -8.2/-17.0% in the three groups respectively. Baseline BMI, reductions in BMI and % change in weight were not statistically different among the groups. Resolution and/or improvement also occurred in other pre-existing co-morbidities measured: type 2 diabetes (86%), hyperlipidemia (57%), depression (71%), obstructive sleep apnea (69%) and GERD (93%). QOL as measured by the Obesity and Weight Loss Quality of Life instrument also improved. In summary, HTN medication requirements were reduced in severely obese patients after surgical intervention with the LAP-BAND AP® system. These improvements tended to be

greater in subjects with a greater % change in weight, but this was not statistically different. Other obesity-related co-morbidities also improved. These data suggest that adjustable gastric banding offers an important adjunctive therapeutic approach to severely obese patients with HTN which may also lead to clinically meaningful reductions in multiple obesity-related co-morbidities.

Keywords: Obesity; Weight loss; Resolution of hypertension; Surgical therapy

PO-337

INITIAL ALISKIREN/HCTZ COMBINATION THERAPY LOWERS BP IN OBESE PATIENTS WITH STAGE 2 HYPERTENSION AND TYPE 2 DIABETES

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Obese patients with stage 2 hypertension and diabetes mellitus (DM) are at high cardio-renal risk. Large BP reductions to reach BP goal, requiring treatment with ≥2 drugs, are often needed. This was a subgroup analysis of patients with BMI ≥ 30 kg/m^2 from an 8-week study of stage 2 hypertension (mean sitting systolic BP [msSBP] 160 to <200 mm Hg) and DM. Eight hundred and sixty patients (BMI ≥ 30 kg/m^2: 607 patients with mean age 58 years and 70% Caucasian) were randomized to aliskiren/hydrochlorothiazide (ALI/HCTZ) 150/12.5 mg single-pill combination (SPC) therapy or amlodipine (AML) 5 mg alone; doses were doubled after 1 week and treatment continued for another 7 weeks. SBP summary statistics by BMI subgroup were predefined; DBP summary statistics were calculated post hoc. Between-treatment analyses were performed post hoc, by ANCOVA for changes in BP and logistic regression for BP control. After 8 weeks, ALI/HCTZ provided larger msSBP reductions from baseline than AML in obese patients (Table), with a significant additional least-squares mean reduction of 2.6 mm Hg (95% CI 0.2, 4.9; $P < 0.05$). ALI/HCTZ showed a trend towards larger msSBP reductions than AML in non-obese patients, although this was not statistically significant. BP control rates were significantly greater with ALI/HCTZ than AML regardless of BMI. Both treatments were generally well tolerated; rates of peripheral edema were higher with AML than ALI/HCTZ (obese 16.7% vs 2.6%; non-obese 15.2% vs 0.8%). In conclusion, ALI/HCTZ 300/25 mg provided significantly larger SBP reductions and greater BP control rates than AML 10 mg after 8 weeks' treatment in obese patients with stage 2 hypertension and DM. Aliskiren/HCTZ SPC therapy represents an important potential treatment for hypertension in these high-risk patients.

	BMI <30 kg/m^2		BMI ≥ 30 kg/m^2	
	ALI/HCTZ 300/25 mg (n = 118)	AML 10 mg (n = 130)	ALI/HCTZ 300/25 mg (n = 306)	AML 10 mg (n = 299)
Mean baseline BP, mm Hg	168.5/89.4	167.8/89.1	167.8/92.2	167.2/92.2
Change from baseline at week 8 endpoint, mm Hg (least-squares mean ± SEM)				
msSBP	-28.6 ± 1.4	-26.0 ± 1.3	-28.9 ± 0.9*	-26.3 ± 0.9
msDBP	-10.2 ± 0.8	-9.9 ± 0.7	-9.8 ± 0.5	-8.6 ± 0.5
BP control (<130/80 mm Hg), %	24.6†	13.1	22.9†	14.0

*$P < 0.05$, †$P < 0.01$ vs AML.

Keywords: Direct renin inhibitor; Diabetes; Obesity

PO-338

ALISKIREN/HCTZ INHIBITS RAAS ACTIVITY IN OBESE AND NON-OBESE PATIENTS WITH STAGE 2 HYPERTENSION AND TYPE 2 DIABETES

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Chronic activation of the renin–angiotensin–aldosterone system (RAAS) has been implicated in the development of hypertension and organ damage in patients with type 2 diabetes mellitus (DM) and obesity. The direct renin inhibitor aliskiren targets the RAAS at the rate-limiting step thus reducing plasma renin activity (PRA) and all downstream components. This post hoc analysis assessed the effects on PRA and plasma renin concentration (PRC) of single-pill combination (SPC) therapy with aliskiren and hydrochlorothiazide (ALI/HCTZ) compared with amlodipine (AML) monotherapy in the obese and non-obese subgroups (BMI ≥ 30 and <30 kg/m^2) from an 8-week study in patients with stage 2 hypertension (mean sitting systolic BP [msSBP] 160 to <200 mm Hg) and DM. After a 1- to 4-week washout period, 860 patients were randomized to ALI/HCTZ 150/12.5 mg or AML 5 mg for 1 week, followed by double the doses for another 7 weeks. PRA and PRC were assessed at baseline and week 8. Between-treatment differences were assessed by ANCOVA. At week 8, ALI/HCTZ reduced PRA from baseline by 58%, whereas AML increased PRA by 71% ($P < 0.0001$; Table) in patients with obesity. ALI/HCTZ also reduced PRA in patients without obesity. Both treatments increased PRC from baseline regardless of obesity, but the rises were significantly greater with ALI/HCTZ than AML. In conclusion, ALI/HCTZ provided effective reductions in PRA in patients with stage 2 hypertension and DM, regardless of BMI and despite the observed increases in PRC. These results indicate that aliskiren/HCTZ SPC therapy may be a useful treatment to reduce RAAS activity in patients with DM and hypertension.

	BMI<30 kg/m^2		BMI ≥ 30 kg/m^2	
	ALI/HCTZ 300/25 mg	AML 10 mg	ALI/HCTZ 300/25 mg	AML 10 mg
n	88	84	228	216
Baseline PRA, ng/mL/h	0.4 (0.3, 0.5)	0.4 (0.3, 0.6)	0.5 (0.4, 0.6)	0.4 (0.4, 0.5)
ΔPRA, %	-58* (-65, -50)	67 (39, 100)	-58* (-62 ,-53)	71 (53, 92)
n	89	84	225	215
Baseline PRC, ng/L	5.7 (4.6, 7.1)	5.7 (4.4, 7.2)	6.3 (5.5, 7.2)	4.9 (4.3, 5.6)
ΔPRC, %	845* (677, 1049)	47 (20, 80)	910* (793, 1042)	42 (25, 62)

Baseline data are shown as geometric mean (95% CI). Changes shown as geometric least-squares mean for endpoint/baseline at week 8 (95% CI). *$P < 0.0001$ vs AML.

Keywords: Direct renin inhibitor; Obesity; Diabetes; RAAS

PO-339

ALISKIREN/AMLODIPINE COMBINATION LOWERS BP IN OBESE AND NON-OBESE PATIENTS WITH MODERATE-TO-SEVERE HYPERTENSION

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Obese patients with moderate-to-severe hypertension are at particularly high risk of cardiovascular morbidity and mortality. Current treatment guidelines recommend the first-line use of combination therapy in patients with substantially elevated blood pressure (BP). This study assessed the antihypertensive efficacy of aliskiren/amlodipine (ALI/AML) combination compared with AML monotherapy in obese (BMI $\geq$ 30 kg/m^2) and non-obese (BMI < 30 kg/m^2) patients with moderate-to-severe hypertension. This was an 8-week, multicenter, randomized, double-blind study. After a 1- to 4-week washout period, patients with mean sitting systolic BP (msSBP) $\geq$160 to <200 mm Hg were randomized to receive ALI/AML 150/5 mg or AML 5 mg for 1 week followed by forced titration to ALI/AML 300/10 mg or AML 10 mg for 7 weeks. At week 8, change from baseline in mean sitting BP and the proportion of patients achieving BP control (<140/90 mm Hg) were assessed post hoc in obese and non-obese subgroups. Patient demographics and baseline BP (obese 169.8/95.5 mm Hg [n = 179]; non-obese 172.3/94.7 mm Hg [n = 303]) were similar in the two subgroups. At endpoint, ALI/AML significantly lowered BP compared with AML alone in obese (least-squares mean [LSM] -35.9/-15.1 vs -30.0/-10.9 mm Hg; $P < 0.01$) and non-obese patients (LSM -38.8/-16.8 vs -31.1/-13.3 mm Hg; $P < 0.001$). ALI/AML resulted in significantly greater BP control rates than AML in obese (61.9% vs 46.1%; $P < 0.05$) and non-obese patients (69.4% vs 51.4%; $P < 0.05$). Both treatments were generally well tolerated in each subgroup. In conclusion, these results suggest that treatment with aliskiren/amlodipine combination therapy resulted in significantly greater BP reductions and control rates than amlodipine monotherapy in both obese and non-obese patients with moderate-to-severe hypertension.

Keywords: Direct renin inhibitor; Obesity; Combination therapy; Blood pressure

Patient-Provider-Healthcare System Issues

PO-340

CLINICAL INERTIA IN HYPERTENSION: IDENTIFYING BARRIERS TO IMPROVE QUALITY

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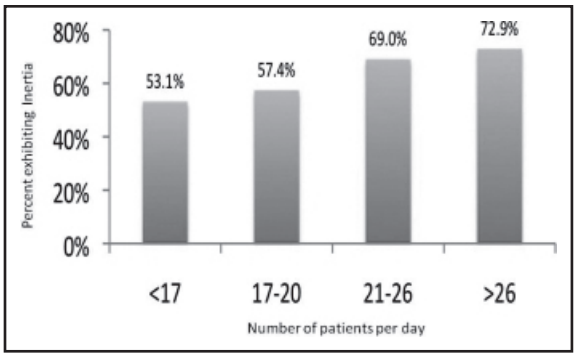
Despite increased treatments and improved provider and patient knowledge of hypertension management benefits, blood pressure (BP) control rates remain suboptimal. This study examines BP control rates and clinical inertia or a clinician's failure to initiate appropriate therapeutic intensification as a possible barrier to BP goal attainment in a COSEHC Cardiovascular Center of Excellence multi-specialty primary care clinic. Hypertensive outpatients were identified using ICD-9 diagnosis codes of 401.0, 401.1, and 401.9. EMR data including provider and patient demographics, BP measurements, diabetic status, medications, insurance, and action profiles related to change in BP therapeutic regimens during the visit were extracted from 32 individual patient visits for each of the 57 primary care providers (n = 1824 visits). This clinic possessed lower hypertension control rates (BP < 140/90 mm Hg or <130/80 mm Hg, diabetic) for all patients (52%) and diabetic patients (26%) as compared to HEDIS Medicaid, Medicare, and Commercial BP control rates (56%, 59%, and 63% respectively for all patients and 31%, 32%, 33% respectively for diabetic patients). Of patients not obtaining BP goals, no action was taken in 63% of cases. Statistically significant inertia was exhibited most often by increased provider patient volume with inertia exhibited 73% of the time in providers seeing >26 patients per day (Figure 1). There was significantly greater inertia in individuals possessing BP < 10 mm Hg above goal (71%), diabetic patients (70%) as compared to non-diabetics (57%), and non-Hispanic whites (66%) as compared to African Americans (52%). For hypertension control rates to improve nationwide, physicians should be cognizant of clinical inertia in their daily practice evaluating patient volume, ethnicity, diabetic status, and the magnitude of BP elevation above goal as they determine if and how to intensify therapeutic treatment. This information will be the basis for individual physician process improvement interventions to reduce inertia for achieving BP goals.



Keywords: Inertia; Blood pressure; Hypertension; Clinica inertia

PO-341

RENAL ARTERY STENT MANAGEMENT: A SURVEY OF LOCAL PRACTICE PATTERNS

Frank K. Boateng, Daniel L. Landry, Barbara A. Greco. Baystate Medical Center, Springfield, MA.

The number of percutaneous renal artery stent (PTRS) interventions has risen over the past decade despite controversy regarding clinical benefits. In-stent stenosis (ISS) occurs commonly and follow-up care of these patients is not standardized. The purpose of this study was to assess the practice pattern among physicians involved in the care of patients undergoing PTRS in our area.

Method: A survey was distributed electronically to physicians involved in the care of patients with renal artery stenosis (RAS) at Baystate Medical Center. Questions were designed to query practices regarding pre- and post-PTRS management.

Results: Response rate was 44.5% of 101 surveyed physicians: 18 nephrologists, 14 hospitalists and internists, four vascular surgeons, four interventionalists (IR), and two noninvasive

cardiologists. There was significant variability among responders in follow up, duration of anti-platelet therapy, statin use, ISS screening indications, intervals, and modality. Twenty eight percent felt the referring physician should consent the patient for PTRS and 83% supported the need for a standardized consent form providing detailed, evidence based data regarding the chance of clinical response and risk of ISS.

Conclusion: This survey reveals significant variability among physicians in the management of patients with RAS undergoing PTRS and supports the need for standardization to allow for outcome assessment and quality improvement.

Table I: Selected survey responses

Consent	%	%	%	%
Who should consent	IR 72	Referring* 28		
Need standardized form	Yes 83	No 17		
Post-PTRS care				
Stent card provided	Yes 63	No 37		
Routine Cr check	Yes 93	No 7		
Time Cr check	24–48 hours 74	<24 hours 13	>1 week 13	
Clinical follow up	2–3 days 17	1–2 weeks 71	1–3 months 12	
Duration of antiplatelet Rx	4–6 weeks 22	3 months 44	1 year** 11	
Statin use	Yes 68	No 32		
Screening for ISS				
Who is responsible	Referring* 76	IR 17	Other 7	
Clinical follow up interval	Q1–3 months 35	Qmonths 44	Q12 months 13	Other 8
Basis for ISS screening	Clinical 71	Routine 29		
Screening modality	DUS 69	CTA 17	MRA 8	Angio 6

*MD who sent pt for stent;**22% deferred to other MD; cr-creatinine.

Keywords: Renal artery stenosis; Renal artery stent; Renal artery in-stent stenosis; Renal artery stent management

PO-342

IMPACT OF SWITCHING FROM VALSARTAN TO A LOWER-TIERED ANGIOTENSIN RECEPTOR BLOCKER ON SUBSEQUENT TREATMENT PATTERNS

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Background: In 2009, a health plan moved valsartan-based angiotensin receptor blockers (ARBs) from Tier 2 to the more expensive Tier 3 on the preferred drug list (PDL), while other ARBs remained on Tier 2.

Objective: Evaluate the impact of switching from valsartan to a Tier 2 ARB on subsequent treatment patterns.

Methods: Hypertensive patients persistent on valsartan in 2008 who either continued on valsartan or switched to a Tier 2 ARB (olmesartan, losartan, telmisartan) in 2009 were identified from a US commercial claims database. The date of the first valsartan or Tier 2 ARB fill in 2009 was the index date and the ARB filled was the index ARB. Outcomes included discontinuation, defined as a >60 day gap in therapy, and adherence, calculated as the proportion of days covered (PDC), in the 6 month follow-up period. Patients who switched to a Tier 2 ARB were matched to patients who continued valsartan. Statistical comparisons were made between cohorts using tests for paired data. Logistic regression of outcomes was conducted.

Results: Two thousand two hundred and seventy-five Tier 2 ARB users were matched to 2275 valsartan continuers. Demographics and baseline measures (comorbidity, antihypertensive therapy, health care utilization and costs) were not statistically significantly different between the cohorts. The rate of index ARB discontinuation was significantly lower among valsartan continuers (6%) compared to patients filling Tier 2 ARBs (10%; $P < 0.001$). After adjusting for confounders, patients who switched to a Tier 2 ARB were twice as likely to discontinue compared to valsartan users (OR = 2.02; 95% CI = 1.57–2.60). Average PDC was higher in patients who switched to a Tier 2 ARB (0.87) compared to valsartan users (0.85; $P = 0.004$). In a logistic regression of PDC $\geq$ 0.9 vs PDC $<$ 0.9, patients who switched to a Tier 2 ARB were not significantly more likely to have PDC $\geq$ 0.9 compared to patients who continued valsartan (OR = 0.89; 95% CI = 0.77–1.03).

Conclusions: Patients who switched to a Tier 2 ARB following the up-tiering of valsartan were more likely to discontinue their index ARB compared to patients that continued on valsartan, indicating that PDL tier placement may impact subsequent ARB use patterns. Additional research to assess the long-term impact of a tier change is warranted.

Keywords: Angiotensin receptor blocker; Treatment patterns; Adherence

PO-343

HYPERTENSION SPECIALISTS' CURRENT AND POTENTIAL IMPACT ON RESISTANT HYPERTENSION IN THE MEDICARE POPULATION

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With a proposed budget of $476 billion in fiscal 2011, Medicare will cover part of the medical expenses of 48.1 million Americans, the majority of whom are older than 65 years of age. The National Committee on Quality Assurance has highlighted blood pressure (BP) control as the medical intervention that would save the most lives and hospital costs. To assess the current and potential impact of ASH-Certified Hypertension Specialists (ACHS) on resistant hypertension (RH, with a presumed prevalence of 15–20% in American hypertensives), we surveyed (via electronic mail) all current ACHS residing in the USA regarding the prevalence of RH and Medicare beneficiaries with it in their practices. The response rate was 277/1324, or 21%. On average, ACHS report spending 38 (interquartile range [IQR]: 15) hours/week in practice, seeing about 1250 (IQR: 2250) unique patients annually. About 11 (IQR: 16.5) hours/week are devoted to caring for resistant or complex hypertensive patients, either self-referred or referred from another healthcare provider, or about 250 (IQR: 375) unique patients/year. Of these, about 135 (IQR: 188) complex or resistant hypertensive patients are covered by Medicare. These data suggest that Medicare currently covers about 179,000 resistant hypertensives seen by ACHS. Other data indicate that ACHS have achieved BP control in 55% of referred patients with RH. If Medicare were to encourage its beneficiaries with RH to be seen by ACHS by enhancing reimbursement for ACHS, approximately 2.5–3.4 million Americans with RH in the Medicare age group would achieve BP control. This could have important ramifications for the ACHS workforce.

Keywords: Taxonomy code for hypertension specialist; ASH-certified hypertension specialist; Complex and/or resistant hypertension; Physician workforce

PO-344

MITIGATING RISK – CARDIOVASCULAR HEALTH ASSESSMENT FOR THE MEN/MS OF PATERSON AND PASSAIC COUNTY – MR CHAMMP

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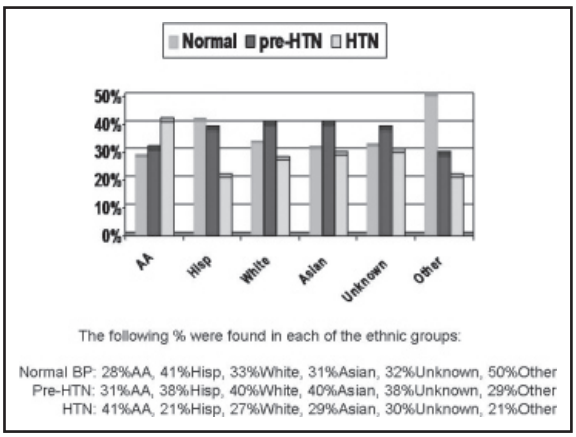
The purpose of MR CHAMMP (Mititgating Risk – Cardiac Health Assessment for the Men/Ms. of Paterson and Passaic County) is to develop and sustain a community-based (CB) screening, education and access to care (SEA) hypertension (HTN) program for all people in Paterson, NJ (pop. 148,708 – 50% Hispanic, 33% Black, 22% below poverty level (BPL) and Passaic County, NJ (pop. 491,778 – 36% Hispanic and 15% Black, 14% BPL) with special emphasis on minority populations. Methods include: (1) Weekly community outreach programs; (2) Identifying urban populations who may be at risk for HTN; and (3) Training site specific key community leaders (KCL). KCL are SEA trained so that cultural, language and ethnic specific (CLES), independent, ongoing programs are conducted at community sites (faith-based, employment, shelters, senior citizen housing, etc.) where people live and congregate. Each participant is provided with a form that includes their categorical BP recordings, predictors of HTN and cardiovascular disease, recommendations for follow-up and numbers to call for access to care (ATC). From October 2009 to November 2010, 50 MR CHAMMP programs were given including the establishment of six community CLES independent sites. A total of 1610 people were educated and 1414 were screened (249 Black, 434 Hispanic, 358 White, 124 Asian, 235 Unknown and 14 Other) (Figure 1).

Conclusions: (1) A community based cultural, language and ethnic specific, screening, education and access to care hypertension program can be established with key community leaders; (2) Pre-hypertension is present in up to 40% of this population; (3) Up to 72% of Blacks and up to 59% of Hispanics have elevated BP; (4) Urban and minority populations are in need of ongoing community based programs to identify pre-HTN and HTN and provide access to care and (5) Future work is needed to identify people who sought care, obtained treatment, reached goal BP, and identify people who suffered adverse cardiovascualr outcomes.



Keywords: Community screening; Innovative program; Hypertension idenification; Hypertension access to care

PO-345

QUANTIFICATION OF CLINICAL INERTIA DURING GP'S MANAGEMENT OF UNCONTROLLED HYPERTENSIVE PATIENTS-CLEPSYDRE STUDY

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To assess therapeutic inertia during the management of uncontrolled hypertensive patients (pts) [blood pressure (BP) $\geq$140/90 for non diabetic (DB) and BP $\geq$ 130/80 mm Hg for DB pts].
French cross sectional study conducted with 1419 GPs in 2010. Each physician included the first five consecutive hypertensive pts according to above inclusion criteria. The therapeutic score (TS) was defined for each pt according to the number of antihypertensive classes prescribed before and after the consultation and this TS evolution was considered as a clinical inertia marker. Univariate and multivariate analysis (logistic model) were performed to determine factors which could influence the decision.
Six thousand nine hundred and twenty-four pts were included. Mean age was 63 $\pm$ 11 years and 56% were men. Mean BP was 160 $\pm$ 12/92 $\pm$ 9 mm Hg, 53% had moderate and 12% severe HTN. Twenty-five percent of the pts were DB, 29% were obese, 60% had dyslipidemia and <10% had a coronary heart disease (CHD). More than 90% of the pts were treated: with a single-drug therapy for 43%, a two-drug therapy for 38% and 19% with a three-drug therapy or more. Among the last ones, only 47% received a combination of a diuretic, a renin angiotensin system inhibitor and a calcium channel blocker. The treatment was changed for 94.7% of the pts but the TS was unchanged in 62.2% (mainly switch to other antihypertensive class(es) or increase the dosage of the current treatment). The TS was increased in only 37.6% of the pts and decreased in 0.2%. In the multivariate analysis, more recent and more severe HTN, a low baseline TS, active tobacco use, CHD and lack of dyslipidemia were predictive for deciding to increase the TS.
Nearly half of the uncontrolled hypertensive pts are treated with only a single-drug therapy. The most frequent therapeutic decision for these uncontrolled pts is to maintain the same TS. On the contrary another therapeutic class is added for only one third of the pts. This study demonstrated that clinical therapeutic inertia is important in the GPs management of uncontrolled hypertensive pts.

Keywords: Clinical intertia; Uncontrolled hypertension; General practitioner

PO-346

TIME TO TALK CARDIO COMMUNICATION TOOL USE IMPROVES CARDIOVASCULAR DISEASE MANAGEMENT BEHAVIORS AND SATISFACTION

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Cardiovascular disease (CVD) is a leading cause of death in the United States. Communication skill building is key in building better provider/patient relationships that address CVD education and adherence challenges. Time to Talk CARDIO is a program with web-based learning objectives that is dedicated to

advancing CVD health by improving patient-health care provider dialogue. The program uses a communication skill-building tool called LEAPS (Listen, Educate, Assess, Partner, Support). A North Carolina physician along with his clinic, Access Healthcare, a COSEHC Cardiovascular Center of Excellence™ participated as a pilot test site for the Time to Talk CARDIO communication tool. The objective was to determine changes in patient and provider self report of satisfaction and LEAP skills subscales following visit communication after utilization of the Time to Talk CARDIO website video curriculum and goal setting worksheets using a pre/post test questionnaire. Patients and providers participated in LEAP skills and satisfaction surveys. Paired *t*-test (significance = $P < 0.05$) were used to compare scores prior to and following use of the Time to Talk CARDIO resources. There were statistically significant improvements in four of six patient LEAPS behavior subscales (concerns expressed, ability to follow, shared decision making, interpersonal rapport), four of six provider LEAPS behavior subscales (patient education, influence patient adherence behavior, shared decision making, interpersonal rapport), all six patient satisfaction subscales (understanding, time satisfaction, ability to follow recommendations, satisfaction with concerns recognized, shared decision making, interpersonal rapport), and all six provider satisfaction subscales (data gathering skills, time management, patient education, influence patient adherence behavior, shared decision making, interpersonal rapport). These pilot test results suggest the use of the Time to Talk CARDIO communication building tools and website improves patient and provider behavior and satisfaction levels. Use of these tools could positively impact dialogue between patients and providers related to CVD management and engage both groups in improving dialogue through skill-building training.

Keywords: Patient/provider communication; Cardiovascular disease; Behavior; Satisfaction

PO-347

AUTOMATED OUTREACH FOR ANTIHYPERTENSIVE MEDICATION REFILL REMINDERS

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An automated telephone system reminding patients with hypertension to obtain overdue antihypertensive medication refills was evaluated in a large, diverse integrated health care system. All participants were members of Kaiser Permanente Southern California. Participants were ≥18 years of age with hypertension identified from a case-identification database. Participants had a prescription for lisinopril and hydrochlorothiazide combination overdue for refill between 2 and 6 weeks. Participants were randomly assigned to either an automated telephone outreach or a control group (usual care). The outreach consisted of an automated telephone call that instructed the member to order a refill for their overdue prescription by calling the number on their medication bottle or by using the Kaiser Permanente online refill system. The primary outcome was refill rate at 2 weeks among the two groups. The number randomized was 4182 in the control group and 4124 in the outreach group. The refill rate at 2 weeks was 22.9% in the control group and 28.6% in the outreach group (difference 5.7%; $P < 0.001$). This low-cost outreach intervention of automated prescription refill reminders resulted in a significant increase in refill rates. Further analyses will examine varying durations of being overdue for refill and the reminder call as well as medication adherence and persistence and blood pressure control in this population.

Keywords: Automated refill reminder; Adherence; Antihypertensive medication; Intervention

PO-348

IMPACT OF NON-MEDICAL SWITCHING BETWEEN DIFFERENT ANGIOTENSIN RECEPTOR BLOCKERS (ARB) ON BLOOD PRESSURE AND MEDICAL RESOURCE UTILIZATION

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Background: The classic "step therapy" of one drug titrated at a time to reduce blood pressure (BP) is inadequate in achieving BP control in patients with uncontrolled hypertension or those with compelling indications (e.g. diabetes and chronic kidney disease). Consequently, such patients often require multiple titrations and/or combination therapy to improve BP goal-attainment rates. However, changes to patient's antihypertensive drug regimen, could potentially result in loss of BP control, increase in adverse events, and even increased treatment costs.

Objective: To assess the impact of angiotensin receptors blockers (ARBs) switch on changes in BP; and if switching required an increase in office visits and other antihypertensive medications.

Methods: A retrospective analysis was conducted using the GE Centricity electronic medical records of a primary care physician group. Hypertensive patients >18 years, continuously enrolled, and receiving ARB therapy were included. Switch must have occurred after the patient was on the first ARB for at least 60 days. The control group remained on the same ARB and did not switch. A 1:1 matching was done on the duration of initial ARB therapy and presence of diabetes/renal impairment.

Results: Four thousand eight hundred and fifty-one patients were prescribed an ARB between 2004 and 2008. Switchers (n = 129) and control group (n = 134) with controlled BP at baseline (<130/80 diabetes/renal impairment; <140/90 all others) were extracted from 714 matched pairs. There was no difference in mean baseline SBP for switchers (125.55 + 13.84) and control (124.25 + 11.42) but switchers had higher post-switch SBP (131.94 + 14.39) than control (127.74 + 15.04) ($P = 0.022$). More switchers lost control from index to first visit post-index period (31.8%) than control (23.1%). More antihypertensive agents were added in switchers (1.58 + 1.5) than control (0.98 + 1.1) in the post-index period ($P < 0.001$).

Conclusions: Non-therapeutic switches may result in loss of BP control and additional medical resource use and cost. Careful consideration should be given before switching ARB therapy for non-therapeutic reasons such as formulary changes or drug availability.

Keywords: Angiotensin receptor blockers; Switching; Resource utilization; Hypertension

PO-349

WITHDRAWN AT AUTHORS' REQUEST

PO-350

SIMPLE DRUG PREFERENCE QUESTIONS ARE PREDICTIVE OF ANTIHYPERTENSIVE RESPONSE: A STITCH2 SUBSTUDY

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Patient behavior is a major determinant of blood pressure (BP) control. However, the value of questionnaire-based behavioral assessments as predictors of response to antihypertensive treatment is unclear. Therefore we assessed the relationship between responses to a 15 item self-administered questionnaire [modified from the Expectations and Satisfaction with Treatment Questionnaire (ESTQ)] and clinical outcomes.

Patients from the STITCH2 study, a cluster randomized controlled trial of a simplified comprehensive treatment algorithm for the management of hypertension and dyslipidemia, were asked to complete the modified ESTQ at study entry and after 6 months of follow-up. The baseline survey was completed by 1038 eligible patients (98%) who had either above-target BP (predominantly systolic) and/or LDL cholesterol. Responses from the baseline survey were explored to assess correlation with BP and LDL-C reduction.

Baseline responses to two of the 15 questions relating to comfort with drug switching and with frequency of drug taking were significantly correlated with change in systolic BP, and one question related to concern with number of prescribed medications was significantly correlated with change in diastolic BP. These three questions were dichotomized and reviewed within the subsamples of patients with either BP or LDL-C above target. In patients with uncontrolled hypertension at entry, those with positive responses demonstrated significantly greater systolic BP reductions over the 6 month study for two questions related to drug switching and frequency compared to those who responded as neutral or negative (Difference in systolic BP reduction of 7.4 mm Hg, 95% CI: 4.7–10.1 mm Hg and 4.3 mm Hg, 95% CI: 1.6–7.0 mm Hg, respectively; $P < 0.001$ for both questions). In the third question, patients with responses indicating greater concern with taking too many medications demonstrated a significantly lesser diastolic BP reduction compared to neutral or unconcerned responses (Difference in diastolic BP reduction of -2.5 mm Hg, 95% CI -4.3 to −0.7 mm Hg; $P = 0.006$). In contrast, none of the 15 baseline questions were predictive of reductions in LDL-C. These data indicate that a simple behavioral assessment may predict response to antihypertensive treatment.

Keywords: Hypertension; Patient satisfaction; Antihypertensive medication; Patient survey

PO-351

INCREASED CLINICAL OUTCOMES AT 1 YEAR FOLLOW-UP FOUND IN A DIABETIC PATIENT-CENTERED MEDICAL HOME PILOT PROGRAM

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Palmetto Primary Care Physicians (PPCP) partnered with BlueCross BlueShield of SC and BlueChoice HealthPlan to pilot launch a diabetic patient-centered medical home (PCMH). PPCP includes a network of 23 sites in SC. Active PPCP patients diagnosed with diabetes or diabetic complications were entered using a patient registry. The program officially launched April 1, 2009 (baseline) with a series of patient mailings and telephonic outreach and concluded March 31, 2010 (follow-up). Concurrent with program launch and conclusion, PPCP, a COSEHC Cardiovascular Center of Excellence™, provided BlueCross and BlueChoice HealthPlan with patient baseline and follow-up data for glycated hemoglobin (HbA1c), blood pressure, LDL cholesterol, microalbumin (mAb), body mass index (BMI), and eye exam. Baseline and follow-up clinical values on 780 continuously enrolled participants were

analyzed. PPCP measured the greatest percent change and maximized pay for performance on four of 10 measures including, the percent of medical home participants with: (1) LDL levels <100 mg/dL (22% change); (2) an mAb test (27% change); (3) an annual eye exam (19% change); (4) an improved BMI since baseline. Participants with a HbA1c test and a HbA1c <8% improved by 5% and 3% respectively. Utilization outcomes measures showed a decrease percent change by 10%, 12%, and 27% respectively in the number of inpatient days, emergency room visits, and observation admissions. These percent change values were even more striking as compared to a like control group. There was also a decrease in total medical/pharmacy costs (despite increased pharmacy charges due to higher prescription adherence), inpatient hospital visits, inpatient specialty care costs, and ancillary costs by 7%, 10%, 11%, and 19% respectively in the pilot PCMH group as compared to the control group. There was a 7% per member per month cost decrease and a 16% risk adjusted cost savings. In conclusion, PPCP's pilot program with BlueCross and Blue Choice HealthPlan demonstrates that a PCMH has significant impact on improving population process and outcomes measures specific to diabetes. This program represents a model that can be expanded to include multiple chronic disease states and payors.

Keywords: Medical home; Diabetes

PO-352

SINGLE PILL VS FREE-EQUIVALENT COMBINATION THERAPIES FOR HYPERTENSION: META-ANALYSIS OF ADHERENCE AND COSTS

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Previous research has demonstrated improved adherence to antihypertensive treatment regimens that combine two or more active agents in a single pill combination (SPC).

A meta-analyses was conducted to estimate differences in health care costs, adherence, and persistence between SPC and free-equivalent combinations (FEC) of medications used to treat hypertension.

A structured review and meta-analysis of studies identified from PubMed and EMBASE, which compared SPC anti-hypertensive agents vs FEC was conducted. There was no date limit on the literature search. Studies comparing these regimens in terms of costs, or adherence and persistence were considered. Costs were expressed in 2009 $USD. Adherence/compliance was reported as medication possession ratios (MPR) and persistence as proportion of patients who filled prescriptions within a given timeframe. Random effects meta-analyses are presented as pooled mean differences for continuous outcomes and as pooled risk ratios for categorical outcomes with 95% confidence intervals (CI).

The search yielded 12 retrospective studies that met the inclusion criteria. Seven studies presenting total annual all cause health care costs or hypertension-related costs, showed lower costs with SPC than FEC; the difference on average was $1357 (CI $778, $1935). Overall pharmacy costs were reported and were lower for SPC by $605 (CI $376, 835) in three studies, but the pooled difference for hypertension-related medication costs was not significant. Adherence was better for patients on SPC vs FEC with an average difference in MPR of 13% (CI 8, 18%) in eight studies that reported this outcome. Persistence was higher in all SPC vs FEC comparisons with a pooled risk ratio = 2.1 (CI 1.1, 4.1). Heterogeneity was noted in analyses of all outcomes and sensitivity analyses were conducted.

The results from this meta-analysis showed that patients taking multiple antihypertensive medications as a combined single pill had demonstrably lower all cause and hypertension-related healthcare costs than patients taking several pills as FEC. Adherence and persistence were also significantly greater with SPC than FEC, suggesting that SPC regimens could contribute to cost-effective care.

Keywords: Adherence; Fixed dose combination; Hypertension; Single pill combination

PO-353

DIFFERENCES AND SIMILARITIES IN EXPLANATORY MODELS OF HYPERTENSION IN THE US, TANZANIA AND JAMAICA

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Background: Disease misperceptions may contribute to emergency department (ED) presentation with poorly controlled chronic hypertension (cHTN).

Objectives: (1) To explore disease knowledge in ED patients with cHTN using explanatory modeling; and (2) to compare gaps in cHTN knowledge across racially similar but geographically divergent ED patients.

Methods: ED patients of African origin with cHTN were recruited from three sites: Detroit Receiving Hospital (DRH – Detroit, MI), the Tanzanian Training Center for International Health (TTCIH – Ifakara, TZ) and University Hospital of the West Indies (UHWI – Kingston, JA). Demographic and baseline data were collected along with open-ended responses to a series of questions related to cHTN. Qualitative responses were coded into disease-relevant, quantitative domains by two separate, blinded reviewers (Cohen's $\kappa = 0.99$) and multilevel comparisons were performed using Kruskal–Wallis or ANOVA tests, where appropriate.

Results: One hundred and ninety-seven patients were enrolled - 97 at DRH, 50 at TTCIH, and 50 at UHWI. Demographic data were similar across sites but patients at DRH had a longer mean (SD) duration of cHTN (12.1 [11.0] yrs vs 4.6 [5.8] yrs vs 9.1 [7.6]; $P < 0.0001$), and were less likely to be on antihypertensive therapy (84.5% vs 92% vs 100%, $P = 0.001$). Explanatory models revealed limited recognition of cHTN as a "disease" (19.6% vs 28% vs 16%; $P = 0.31$) and consistency in the belief that cHTN was curable (44.3% vs 36% vs 42%; $P = 0.62$). Stress (48.4% vs 60% vs 50%; $P = 0.31$) and, especially at DRH, diet (62.2% vs 22% vs 36)%; $P < 0.0001$) were identified most frequently as causes of cHTN.

Conclusions: Misperceptions related to cHTN are common in the ED. While specific areas of disconnect exist by geographic region, under-appreciation of cHTN as a dire and fixed disease state is consistent suggesting that a uniform educational intervention may be of benefit in this setting.

Keywords: Explanatory model; Hypertension; African

PO-354

TREAT TO TARGET USING INTERACTIVE VOICE MESSAGING TO ENHANCE PRIMARY CARE PHYSICAN MANAGEMENT OF HYPERTENSION

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The goal of this study was to determine the efficacy of Interactive Voice Recognition (IVR) technology in improving Hypertension control by empowering patients to be involved in the treatment of their hypertension, thereby improving adherence.
The hypothesis was that IVR can be used effectively to provide education, awarenesss, and follow up support for patients with uncontrolled Hypertension.

Study design: 1. Outreach to patients on a hypertension registry whose last BP reading was above goal.
2. To utilize IVR as a virtual health coach, in conjunction with an RN visit, to enhance care systems, through weekly automated patient calls. These calls track home BP readings, medication adherence and medication self titration according to a Hypertension Medical Management Algorithm.

Method: 1. A Computerised Hypertension registry was scanned weekly for patients with last BP elevated 6 weeks previosuly or no BP reading in last 1 year. An IVR call in English or Spanish was made encouraging patients to return to their Primary Care Physicians nurse for a BP check and inviting them to a Hypertension education class.
2. Patients returning with elevated BP attended a Nurse Clinic for education on hypertension and on self titration of anti hypertensive medication following a medication algorithm and based on home BP readings. Enrolled patients recieved an IVR message biweekly for up to 7 weeks eccouraging titration of medication and notifying a nurse coach if not checking BPor if BP too high or too low

Results of first part:
•Sixty-one thousand seven hundred and sixty-six IVR Calls made.
•Fifty-four percent IVR calls authenticated.
•Eighteen percent members returned within 2 weeks for BP check
•Improved overall HTN control rate from 74% to 81% (Sep 08/Jun 09)

Results of second part: Patients referred: 400
Ninety-eight came to initial appointment
45.9% control at initial visit
Of the remainder still not controlled,
Thirteen undertook self Titration with IVR leading to an 84% control at 7 weeks
Twenty-one undertook self Titration without IVR leading to a 66% control rate at 7 weeks
Nineteen Had no self Titration, just nurse education leading to a 53% control at 7 weeks

Conclusion: Interactive voice techonolgy can be used to improve operational efficiency of an outreach program for a large population of hypertensive patients. In addition it can be used to improve the operational efficincy of administration of a patient self titration program for the control of Hypertension.

Keywords: Interactive voice recognition technology; Self titration; Home blood pressure monitoring; Operational efficiency

PO-355

IS POOR BLOOD PRESSURE CONTROL IN PATIENTS PRESENTING FOR ELECTIVE SURGERY PREDICTABLE?

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Anesthesiologists may regard uncontrolled hypertension as a relative contraindication to elective surgery. At our medical center, many patients undergo a pre-operative evaluation, including a BP determination, at an outpatient clinic (Clinic-BP) prior to elective surgery. The next BP obtained for many patients occurs in the operating room immediately prior to induction of anesthesia (OR-BP). We used an electronic database (Centricity®; General Electric Healthcare, Waukesha, WI) maintained by our Department of Anesthesiology to determine whether patients with JNC-7 Stage 2 hypertension in the OR could be reliably identified by pre-operative Clinic-BP screening preformed prior to the day of surgery.

Results: The study sample consisted of 11,831 adults (>18 years old, 60.5 ± 15.1 years, [mean ± SD]) who had both Clinic-BP and OR-BP. Systolic and diastolic OR-BPs (138.9 ± 22.4/74.8 ± 11.4 mm Hg) were higher than Clinic-BPs (134.6 ± 20.1/73.4 ± 11.5 mm Hg, both $P < 0.001$). BPs in the two settings were significantly but only moderately correlated: SBP, $r = 0.51$, $P < 0.001$; DBP, $r = 0.45$, $P < 0.001$).
By JNC-7 criteria, there were 1304 Stage 2 Clinic-BP hypertensives (11.0% of total) and 2140 Stage 2 OR-BP hypertensives (18.1%). Of the 2140 with Stage 2 OR-BP, only 647 (30.2%) were classified as Stage 2 by Clinic-BP. Of the 1304 Stage 2 Clinic-BP hypertensives, 647 (49.6%) were also Stage 2 OR-BP hypertensives.
When we restricted the analysis to patients with SBP ≥ 180 mm Hg systolic or DBP ≥ 100 mm Hg, a subgroup considered to require clinical attention by anesthesiologists at our institution, Clinic-BP identified 371 cases (3.1%) and OR-BP 651 (5.5%). Of the 651 OR-BP cases, 105 (16.1%) had also been ≥180/100 mm Hg on Clinic-BP.

Conclusions: Stage 2 hypertension is frequently encountered immediately prior to elective surgery, where it may cause concern about the advisability of proceeding with administration of anesthesia. Pre-operative screening of BP in an outpatient clinic can identify some patients who will demonstrate Stage 2 hypertension in the holding area, but many will be encountered de novo. More information is needed to understand how best to identify patients whose OR-BP will be elevated and to determine whether elevated OR-BP is a risk factor for perioperative complications.

Keywords: Pre-operative BP; Stage 2 hypertension

Preclinical Models/Experimental Hypertension

PO-356

DYSGLYCEMIA INDUCES ABNORMAL CIRCADIAN VARIABILITY OF BLOOD PRESSURE

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Background: We have shown that in healthy adults prediabetes is associated with abnormal circadian blood pressure variability (abn CBPV).

Hypothesis: We tested the hypothesis that increased blood glucose concentrations induce abn CBPV.

Methods: Dahl salt-sensitive (S) rats (n = 19) were fed either an American diet (AD; Teklad Custom TD.08811-high glycemic index high fat) or a standard diet (SD; TD.08810-low glycemic index low fat) after weaning for 7 weeks. Rats were surgically implanted with C40 transmitters and blood pressure (BP, both systolic; SBP and diastolic; DBP) and heart rate (HR) were recorded by telemetry every 5 minutes for 8 days and nights. Pulse pressure (PP) was calculated (PP = SBP-DBP).

Results: The AD fed group displayed increased fasting blood glucose (FBG) 90.1 (16.9) mg/dL, [mean (SD)] compared to SD fed group 63.7 (5.9) mg/dL, $P = 0.0004$, despite no significant difference in weight 396 (14) vs 388 (17) g, $P = 0.3$. The higher FBG group exhibited elevated overall 8-day mean SBP, DBP ($P = 0.02$) and PP. Mean daily nighttime (active; 6:30 PM–6:25 AM) BP and HR was higher than daytime (rest) period in both groups, but the percent change was significantly higher ($P = 0.001$, 0.01, 0.0001, 0.02, respectively for SBP, DBP, PP and HR) in the group with higher FBG compared to lower FBG.

Conclusion: These data validate our stated hypothesis that increased glucose concentrations result in abn CBPV. Our results provide the fundamental basis for examination of relationship between dysglycemia and activation of mechanisms (adipose tissue dysfunction induced local and systemic inflammation, insulin resistance and alteration of adipose tissue precursors for the renin-aldosterone-angiotensin system) generating abn CBPV.

Keywords: Circadian variability of blood pressure; Fasting blood glucose concentrations; Dysglycemia; RAAS

PO-357

PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS NEURONS PROJECT TO PARASYMPATHETIC BRAINSTEM NEURONS THAT CONTROL HEART RATE

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Descending projections from the paraventricular nucleus of the hypothalamus (PVN) play a major role in the autonomic nervous system control of cardiorespiratory function. PVN neurons have been shown to project to several brainstem sites, including nucleus ambiguus (NA), dorsomotor nucleus of the vagus (DMV), rostral ventrolateral medulla (RVLM) and nucleus of the solitary tract (NTS). While the role of the PVN in sympathetic cardiovascular control is well documented, a role of the PVN in parasympathetic cardiovascular regulation has yet to be tested directly. We have studied the descending PVN projections to brainstem parasympathetic cardiac neurons after microinjecting a lentiviral vector that drives channelrhodopsin-2-EYFP (ChR2-EYFP) fusion protein expression under the synapsin promoter into the PVN of the rat. Confocal microscopy analysis confirms close apposition of ChR2-EYFP fibers to identified cardiac vagal neurons (CVNs) in the NA and DMV. In addition, ChR2-EYFP labeled fibers were detected in the RVLM and NTS. We have also functionally assessed synapses of PVN projections to CVNs using in vitro patch clamp electrophysiology and photoexcitation of ChR2. Photoexcitation of PVN presynaptic terminals evokes an excitatory current in DMV CVNs, mediated by AMPA and NMDA receptors. Our results provide evidence that PVN projections to the brainstem are not limited to sympathetic control, but also include a direct pathway from the PVN to CVNs to activate parasympathetic cardiac neurons.

Keywords: Blood pressure; Heart rate; Hypothalamus; Channelrhodopsin

PO-358

EFFECTS OF SEX ON SYMPATHETIC NEURAL AND HEMODYNAMIC RESPONSES TO HEAD-UP TILT IN HYPERTENSIVE SENIORS

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More elderly women than men have hypertension, and also lower blood pressure (BP) control rate. To test the hypothesis that elderly hypertensive (HT) women have enhanced sympathetic neural responses to orthostasis compared with age-matched HT men. BP, heart rate (HR), cardiac output (Qc), total peripheral resistance (TPR = mean BP/Qc), and muscle sympathetic nerve activity (MSNA) were measured in 16 HT women (mean ± SD; age 67 ± 6 years), 20 HT men (70 ± 5 years), 15 normotensive (NT) women (70 ± 8 years) and 5 NT men (68 ± 7 years) during supine and a graded head-up tilt (HUT; 30° for 5 minutes and 60° for 20 minutes). BP increased during HUT, while the increase was greater in HT women than in HT men and NT men/women ($P < 0.05$ for sex, groups and interaction). Supine HR was higher in HT women than HT men (69 ± 7 vs 62 ± 7 beats/min; $P < 0.05$), but upright HR was not different between sexes, and, therefore, the increase in HR during 60° HUT was lower in women than men (ΔHR 14 ± 8 vs 16 ± 9 beats/min; $P < 0.05$). Although supine Qc index (Qc divided by body surface area) was similar between sexes, its reduction during HUT was greater in HT women than HT men (ΔQc Index −0.73 ± 0.29 vs −0.57 ± 0.20 L/min/m^2; $P < 0.05$). Surprisingly, both supine and upright MSNA was similar between HT men and women, and between NT men and women (supine: 38 ± 10, 42 ± 8, 39 ± 7, and 42 ± 8; 60°: 60 ± 14, 62 ± 11, 60 ± 6, and 59 ± 12 burst/min; $P = 0.90$ for sex, 0.99 for groups, and 0.87 for interaction). TPR increased during HUT; the increase was greater in HT women than HT men (ΔTPR 2550 ± 811 vs 1462 ± 695 dyn's/cm^5/m^2; $P < 0.05$). Vascular transduction (TPR/MSNA) increased in HT women during HUT, but decreased in HT men (ΔVascular transduction 16 ± 14 vs -14 ± 20 units; $P < 0.05$). Thus, elderly hypertensive women had enhanced blood pressure response during orthostasis compared with elderly hypertensive men, which was attributable to a greater peripheral vasoconstriction. It is likely that an augmented sympathetic vascular transduction and/or non-neural vasoconstriction may contribute to the high prevalence of hypertension and low blood pressure control rate in elderly women.

Supported by NIH R01 HL091078.

Keywords: Hypertension; Orthostasis; Muscle sympathetic nerve activity; Sexes

Pregnancy

PO-359

AUTOANTIBODIES TO THE ANGIOTENSIN II TYPE 1 RECEPTOR IN PREECLAMPSIA

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This aim of this study was to resolve the controversy surrounding the occurrence of agonistic autoantibodies to the angiotensin II type 1 receptor (AT1R) in preeclampsia patients. Several studies have reported that IgG isolates from these patients activate the AT1R via interaction with the second extracellular loop and that the agonistic effect can be inhibited by the ARB losartan. A recent study by Leanõs-Miranda (J Hypertens 2010; 28: 834), which failed to confirm this, has put the earlier results in question.

In our study, IgG was isolated from thirty normal male, thirty non-pregnant female and 58 confirmed preeclamptic samples using GammaBind G sepharose. The isolates were tested using a newly available CHO-K1 cell line expressing the human AT1 receptor coupled to the bioluminescent reporter, aequorin and compared to the response of the cells to angiotensin II (AngII). Additionally, the serum samples from each cohort were screened by immunoassay using both the intact receptor and a library of peptides from the second extracellular loop.

In the CHO cell assay, AngII gave a robust dose-response spanning six orders of magnitude (EC50 1 nmol/L) which could be completely inhibited by losartan (IC50 0.2 nmol/L). While this cell-based assay was extremely responsive to AngII, activation of the AT1 receptor by IgG isolates was <10% of the maximal response given by AngII. Regardless, normal and preeclampsia cohorts differed in the level of activation in an unexpected manner. The median response of isolates from normal cohorts was statistically higher than that from the preeclampsia group, which did not differ from the zero AngII control. No AT1R autoantibodies were found in any of the cohorts when screened by immunoassay. A close examination of the CHO cell assay revealed that co-eluting human serum albumin in the IgG isolates correlated to the low level of receptor activation. Further, purified HSA, whether of human or recombinant origin, supplied by several vendors demonstrated a dose-related activation of the receptor (EC50 20 μmol/L) which was inhibited by losartan.

We conclude that there is no evidence to support the premise that agonistic autoantibodies to the AT1 receptor are present in preeclampsia and that any perceived activation of the AT1 receptor by human-derived isolates in previous studies are likely due to artifacts of the assays employed.

Keywords: Preeclampsia; Angiotensin II; Autoantibodies; CHO-cell receptor assay

PO-360

THE CORRELATION BETWEEN THE SERUM TESTOSTERONE LEVEL AND INSULIN SENSITIVITY IN PRE-ECLAMPSIA – ECLAMPSIA SYNDROME

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Pre-eclampsia (PE), Eclampsia (E) Syndrome is a common and morbid complication. Many features of Insulin Resistance (IR) Syndrome have been associated with this condition. This work was undertaken to study the insulin sensetivity and serum testosterone level and their correlation in PE-E Syndrome Compared to normal pregnancy.

The study was conducted on 60 pregnant women, during third trimester, divided into two Groups:

G1:(Control) Included 15 normal pregnant women.

G2: Included 45 PE-E patients, subdivided into:

G2A: Fifteen cases of mild PE.

G2B: Fifteen cases of severe PE.

G2C: Fifteen cases of E.

Both groups were subjected to routine Lab. Investigations, Ultrasound Scan, Estimation of Fasting Serum Total and Free Testosterone, Insulin and Glucose Level. A Ratio of Fasting Glucose to Insulin <4.5 was Consistant with Insulin Resistance.

The Study Revealed that, there was Significant Increase of the Mean Insulin, Total and Free Testosterone Levels in PE-E when compared to Control G. Also, there was Significant Increase in their Levels in cases of Severe PE-E than in Mild PE. Furthermore, there was Significant Higher Percentage of IR Cases in PE-E when Compared to Normal Pregnancy and when E patients Compared to mild and severe PE. Positive Correlations were found between Total, Free Testosterone and Insulin, also between Hyperandrogenemia and IR in different groups and subgroups.

It is Convenient to Conclude that, Hyperandrogenemia, Hyperinsulinemia and IR may Play a Role in the Pathogenesis of PE-E Syndrome. So, Early assessment of IR and hyperandrogenemia could result in primary detection and prevention of this Syndrome. The Subject is still Open for much future validation, in multicenter and on larger study Scale.

Keywords: Pre-eclampsia; Eclampsia; Insulin resistance

PO-361

EFFECTS OF HIGH ALTITUDE AND ANCESTRY ON UTERINE ARTERY (UA) SHEAR STRESS AND BLOOD PRESSURE IN NORMAL PREGNANT VS PREECLAMPTIC WOMEN

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Shear stress = 4*Blood Flow*viscosity/πr^3 and is the most potent physiologic stimulus for elevating endothelial derived NO. We *hypothesized* that gestational rises in uterine blood flow (UBF) will increase UA Shear Stress, but normalization of shear is seen with increases in UA remodeling (i.e. bigger radii). Study 1: We evaluated UA blood velocity and radii using color Doppler ultrasound in nonpregnant [Proliferative (periovulatory) vs Secretory (luteal) phase; n = 156] and pregnant women [12 vs 24–40 weeks; n = 42]. Pregnancy reduced blood pressure and dramatically elevated heart rates. Compared to nonpregnant menstrual phases, viscosity decreased at 12 weeks and more so at 32 weeks of gestation. UA radius was unaltered by the menstrual cycle but greater at 12 weeks (+35%) and 32 weeks-term (+77%). Secretory phase showed UBF and Velocity rising which continued progressively with gestation. By contrast, Shear Stress increased in Secretory (80%), but did not rise further in early pregnancy (demonstrating complete normalization of shear forces); at 32–40 weeks Shear Stress elevated further (131%) due to UBF rises with no change in radius. Study 2: Comparing European migrants to multi-generational Andean natives the latter have reduced incidences of preeclampsia (proteinuric hypertension) and less high altitude-associated reductions in fetal growth. We observed in term pregnancies (35–38 weeks) at low (400 m) and at high altitude (3600 m), reduced UA Shear Stress in Andean vs European women

(n = 30–40/group). Andean women had lower Shear Stress than European in spite of a marginal rise in volumetric UBF because of greater UA radii in Andean. Bigger UA radii and a lower velocity in Andean vs European women accounts for the reduced Shear Stress. Andean women had more Shear Stress normalization associated with greater birth weights and lower blood pressure regardless of altitude. We evaluated 10 Andean decent preeclamptic women (142/100 mm Hg) who showed lower birth weights, UA velocity, volumetric UBF, and UA Shear Stress compared to controls of either ancestry; demonstrating greater downstream impedance and a lack of intrinsic vessel remodeling. Applying bioengineering principles to physiologic measurements yield unique information that may have clinically important translational applications.

Keywords: Shear stress; Blood pressure; Uterine artery; Pregnancy

Salt-Sensitive Mechanisms of Hypertension

PO-362

SILENCING OF PKG1 GENE SENSITIZES VASCULAR SMOOTH MUSCLE CELLS TO MARINOBUFAGENIN: IMPACT ON AGING, FIBROSIS, AND SALT-SENSITIVITY

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Marinobufagenin (MBG), an endogenous Na/K-ATPase (NKA) inhibitor, promotes natriuresis, but causes vasoconstriction and induces fibrosis via PKCδ-dependent inhibition of Fli-1, a transcription factor and a negative regulator of collagen synthesis. In the vasculature, ANP, via cGMP/PKG-1 dependent mechanism, reduces NKA sensitivity to MBG. We hypothesized that vascular smooth muscle cells (VSMC) from aged rats due to down-regulation of ANP/cGMP/PKG-dependent signaling would exhibit heightened sensitivity to the pro-fibrotic effect of MBG. In response to acute NaCl loading, aged (24-month old) Sprague-Dawley rats exhibited exaggerated MBG (5.4 ± 0.4 vs 1.9 ± 0.2 pmol/h; $P < 0.01$) and pressor responses (29 vs 15 mm Hg; $P < 0.01$), as well as greater inhibition of NKA in aorta as compared to young (3-month old) rats. Levels of vascular PKG1 and Fli-1 in aged rats were markedly reduced. In vitro, 1 nmol/L ANP prevented inhibition of vascular NKA by MBG in young, but not in the aged rats. In VSMC from young rats, 1 nmol/L MBG induced down-regulation of Fli-1 and a 1.5-fold increase in the levels of procollagen-1 and collagen-1, and 1 nmol/L ANP blocked this effect. In aged rats, levels of PKG-1 and Fli-1 in VSMC were markedly reduced vs young rats, and 1 nmol/L MBG decreased Fli-1 (60%) and increased level of collagen-1 1.6-fold ($P < 0.01$). In VSMC from aged rats, ANP failed to oppose the pro-fibrotic effect of MBG. Silencing of the PKG-1 gene in VSMC from young rats was associated with a marked increase in the sensitivity of VSMC to the pro-fibrotic effect of MBG; in this setting 1 nmol/L MBG increased levels of collagen-1 2.5-fold ($P < 0.01$). These results demonstrate that the age-associated reduction in vascular PKG1 levels and resultant decline in cGMP signaling lead to the loss of ability of ANP to oppose MBG-induced inhibition of NKA and fibrosis. Silencing of PKG1 mimics effects of aging with respect to sensitivity of VSMC to pro-fibrotic action of cardiotonic steroids.

Keywords: Aging; Na/K-ATPase; Marinobufagenin; Vascular fibrosis

PO-363

HERITABILITY OF NA/K EXCRETION DURING THE SALINE/LASIX PROTOCOL IN AFRICAN AMERICAN TWINS

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The BP response to Na loading/depletion with the Grim-Weinberger "Saline-Lasix" protocol is under genetic control (h2) in African Americans (AA) and Whites. To test the relationship of h2 for BP and h2 for ENa and EK we analyzed BP and ENa and EK collected every 4 hours during the protocol in 26 sets of AA twins (50% MZ and 50% males). On the saline day ~2000 mL of N-saline was infused from 8 to 12 noon. On the Lasix day, diet was 10 mmol/L Na/day, 80 mmol/L K/day and ~40 mg of Lasix was taken PO at 9 AM, 1 and 5 PM. Heritability computations and determination as to whether specific variables achieved statistical significance as covariates, either alone or simultaneously with other variables, was performed using SOLAR.

Descriptive statistics: mean ± SD (range) and were: Age = 27 ± 7 (18–42); BMI = 25 ± 5 (17–43). Baseline BP: $115 \pm 11/67 \pm 11$. SS was 21% and SR 79%. BP, ENa&EK (mM), h2 q 4 hours are tabulated.

For h2 or Genetic correlation: $^{*}P < 0.05$, $^{**}P < 0.01$. NA, not available.

Univariant h2 was significant for SBP but ENa and EK were not significant as covariables in the model. Thus they do not account for the genetic correlation of SBP during the protocol.

Univariate h2 for Na and K were significcant (with age, sex as covariables). As in the table, significant univariate genetic influences on SBP, were almost always associated with significant genetic influences on ENa and EK. However, further analysis suggests that the genetic correlations for SBP do not covary with ENa and EK. Although specific h2 of SBPs were statistically significant, the ENa and EK failed to achieve statistical sign as covariates in the model.

Using the twin model in AAs the BP and ENa and EK response to sodium loading (saline infusion) and sodium depletion (Lasix and low sodium diet) are under strong genetic control. The relationship of the co-variation of these genetic influences on ENa and EK to the heritability of salt sensitivity in AAs remains to be determined.

Keywords: Genetics; Salt sensitiity; Sodium metabolism; Twins

	Saline day						Lasix day					
Time →	8A-N	N-4P	4–8P	8-M	M-4A	4–8A	8A-N	N-4P	4–8P	8-M	M-4A	4–8A
SBP mm Hg	115	122	122	122	117	117	117	114	114	114	112	112
h2 SBP	20**	73**	79**	58**	28**	20	61**	49**	60**	72**.	NA	NA
ENa mmol/L per 4 h	117*	67*	53*	57*	65*	87	62*	56*	37*	25	17	27
h2 ENa	64*	76*	73*	65*	53*	43	57**	54**	57**	28	NA	Na
EK mmol/L per 4 h	42	12	9	10	13	19	8	9	10	16	28	47
h2 EK	24	85**	34*	59**	32**	1	62**	66**	38*	17	NA	NA
G correl ENa-EK	0.78	0.07	0.56*	0.72*	0.69*	0.99	0.68**	0.72**	0.67*	0.27	NA	NA

PO-364

GENDER DIFFERENCE IN THE RELATIONSHIP OF MARINOBUFAGEIN TO SALT-SENSITIVITY OF BLOOD PRESSURE

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Increased production of the endogenous bufadienolide sodium pump inhibitor marinobufagenin (MBG) occurs in pathological states of fluid retention, and in the Dahl-S rats MBG mediates salt-induced hypertension. The aims of the present study were to determine whether MBG and 24-hour blood pressure (BP) co-vary, and to determine the MBG response to a controlled moderate increase of salt intake in humans and its relation to salt-sensitivity of BP. Healthy subjects (20 males and 19 females; 53 ± 11 year) were examined under baseline conditions (NaCl-intake not standardized) and thereafter received 50 mmol NaCl/day for 8 (4 + 4) weeks in provided meals and drinks. In addition, NaCl capsules (100 mmol/day) and corresponding placebo capsules were administered for 4 weeks each in random order. MBG and 24-hour ambulatory BP were measured at baseline, after 4 weeks of 50 mmol/day (low-salt) and after 4 weeks of 150 mmol/day (high-salt). Plasma MBG (P-MBG) and urinary excretion of MBG (UE-MBG) were measured using a competitive fluoroimmunoassay. In males, baseline P-MBG was directly related to baseline 24 hour-BP [$R = 0.47$, $P = 0.04$ for systolic BP (SBP) and $R = 0.56$, $P = 0.01$ for diastolic BP (DBP)], whereas in females baseline P-MBG was only correlated with baseline SBP ($R = 0.60$, $P = 0.007$). Also, baseline UE-MBG in men, but not in women, was correlated with baseline 24 hour-BP ($R = 0.50$, $P = 0.02$ for SBP and $R = 0.50$, $P = 0.03$ for DBP). The shift in dietary salt from low to high caused elevation of SBP and DBP ($P < 0.001$ and $P = 0.004$) in both genders, whereas P-MBG and UE-MBG increased only in males ($P = 0.03$ and $P < 0.05$). Further, in males, the salt-induced increase of P-MBG correlated with the salt-induced increase in 24 hour-BP ($R = 0.56$, $P = 0.01$ for ΔSBP and $R = 0.67$, $P = 0.001$ for ΔDBP), and this BP increase was predicted by both baseline P-MBG ($R = 0.48$, $P < 0.05$ for SBP and $R = 0.47$, $P = 0.04$ for DBP) and baseline UE-MBG ($R = 0.46$, $P = 0.04$ for SBP and $R = 0.53$, $P = 0.02$ for DBP). After high salt diet UE-MBG was positively correlated with SBP in males ($R = 0.52$, $P = 0.02$), but not in females. Moreover, in normotensive females >45 years, UE-MBG was negatively related to SBP ($R = -0.66$, $P = 0.01$) after high-salt. Our data suggest that MBG is an important determinant of BP, and that its reaction to salt and relation to salt-sensitivity of BP differs by gender.

Keywords: Marinobufagenin; Cardiotonic steroids; Salt-sensitivity of blood pressure; Human hypertension

Secondary Hypertension

PO-365

ASSOCIATION OF RENAL ARTERY STENOSIS WITH ACUTE PULMONARY EDEMA IN HYPERTENSIVE PATIENTS

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Background: The correlation of renal artery stenosis (RAS) with acute pulmonary edema (APE) is considered specific for hypertensives with bilateral RAS or on sole functional kidney (SFK) and it was inferred especially from cases in which the renal revascularisation prevented APE recurrence. Objectives:
The main objective of our study was to evaluate the association of RAS with APE among hypertensive patients, with a distinct interest on unilateral stenosis.

Method: A series of 189 hypertensives were investigated in one hospital clinic for RAS suspicion by duplex ultrasonography (87% accuracy for RAS ≥ 60% in our laboratory). Clinical criteria consigned in current guidelines as predictors of RAS were recorded and analysed.

Results: RAS was identified in 29% of cases (55/189): unilateral in 35 cases, bilateral or on SFK in 20 cases. Comparative analysis between hypertensives with and without RAS is presented in Table I.
The association of unilateral RAS with APE was independent of azotemia.

Conclusions: In this study we have found an important prevalence and a significative association of RAS with APE among hypertensive patients, including for unilateral stenosis, independently of renal azotemia. This correlation, very little emphasised so far, is rising new hypothesis of APE pathogenesis in the presence of RAS, beyond that of volume overload.

Table I. Comparative analysis between hypertensives with and without RAS

	Patients with RAS (N = 55)	Patients without RAS (N = 134)	*P* value
Mean age	59 ± 13 year	59 ± 15 year	*P* = ns
Sex (female/male)	24/31	66/68	*P* = ns
Azotemia	13/55 (24%)	29/134 (8%)	*P* = ns
Azotemia under ACEI/ARBs	15/55 (27%)	11/134 (8%)	*P* = 0.001
Abdominal bruit	7/55 (13%)	6/134 (5%)	*P* = 0.06
Vascular disease	45/55 (82%)	63/134 (47%)	*P* = 0.0002
History of APE	12/55 (22%): 8/35 (23%) unilateral RAS; 4/20 (20%) bilateral/SFK RAS	11/134 (8%)	*P* = 0.01 for unilateral stenosis as for bilateral/SFK stenosis

Azotemia = plasma creatinine >1.4 mg/dL – female; >1.5 mg/dL – male; Azotemia under ACEI/ARBs defined as variation >0.25 mg/dL of plasma creatinine; Vascular disease defined by any clinical or paraclinical evidence of coronary artery disease or cerebrovascular disease or peripheral arterial disease.

Keywords: Arterial hypertension; Renal artery stenosis; Acute pulmonary edema

PO-366

BIG ENDOTHELIN-1 AND NITRIC OXID LEVELS IN HYPERTENSIVE ELDERLY WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

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The aim of this study was to evaluate big-endothelin-1 (ET-1) and nitric oxid (NO) plasmatic levels, blood pressure (BP), and body mass index (BMI) in hypertensive elderly patients with and without obstructive sleep apnea (OSA). Thirty-seven hypertensive elderly patients (>60 years-old) were divided in two groups: group 1 (n = 25) with recent diagnosis of OSA (moderate or severe) and group 2 (n = 12) with no sleep disorders, both confirmed by polysomnography and no use of Continuous Positive

Airway Pressure. They had no diabetes, hyperlipidemia, cardiovascular or lung disease, abuse of alcohol, and were no smokers. They were admitted for 24 hour to the Clinical Research Unit of the Clinical Hospital. A 24-hour ambulatory BP monitoring was evaluated (SPACELABS 90027). A sample of arterial blood was collected into a tube prepared with EDTA and aprotinin at 7 PM and at 7 AM, and ET-1 was measured by ELISA (IBL). NO was measured by chemiluminescence method.

Statistical analysis: Fisher's exact test, Student's unpaired *t* test and univariate analysis of variance. Results are expressed as mean/standard-deviation.

Both groups have similar distribution of gender and age. There were no differences between number (group 1: 1.9/0.9 and 2: 2.3/0.9, $P > 0.05$) and classes of antihypertensive drugs, BMI (group 1: 30.3/4.8 pg/mL, 2: 29.0/5.0 pg/mL, $P > 0.05$), wakefulness, sleep, 24-hour BP, and sleep BP dip (group 1 systolic: 8/10 mm Hg, group 2: 6/9 mm Hg, $P > 0.05$; group 1 diastolic BP: 7/6 mm Hg, group 2 diastolic BP: 6/6 mm Hg, $P > 0.05$). NO levels were similar between groups. ET-1 was higher in group 1 only at 7 AM ($P = 0.02$, adjusted for BMI and number of apneas and hypopneas during the sleep period). In conclusion, comparing hypertensive older individuals with controlled BP, ET-1 levels were higher in volunteers with OSA, only after the sleep period.

Supported by FAEPA-HCFMRP-USP.

Keywords: Obstructive sleep apnea; Elderly; Ambulatory blood pressure monitoring; Big endotelina-1

PO-367

PHEOCHROMOCYTOMA AND CORONARY ARTERY DISEASE

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Objective: To determine frequency and peculiarities of coronary artery disease (CAD), myocardial infarction (MI) and MI-like changes in pheochromocytoma (pheo) patients.

Design and Methods: One-hundred and eighty pheo pts (78 male and 102 female, mean age 40.2 ± 12.1 year) were studied retrospectively. Tumors localized in adrenals (right–84, left–75, both–9, extraadrenal–12). Nineteen pts had recurrent pheo. One hundred and seventy-five pts were hypertensive and five normotensive. All pts were operated and pheo was verified as benign (85) and malignant (95) by histology.

Results: In 14 (eight male and six female, mean age 64.5 ± 9.2 year) of 180 pheo pts coronary artery disease was diagnosed following clinical examination, ECG 12, Holter-ECG-monitoring, M-mode echocardiography and coronarography. Seven patients were diagnosed with MI 1–8 years prior to tumor removal.

In two pheo pts the MI-lke changes in ECG and ECHOCG disappeared within 4 days. In 12 patients, MI-like changes disappeared within 3 weeks after pheo removal. Signs of postinfarction cardiosclerosis (LV hypo- and akinesises, ECG signs) remained only in two patients out of 14 after tumor removal. Patients diagnosed with the CAD and patients not diagnosed with the CAD did not statistically differ in gender, tumor morphology and size, type and level of catecholamines secretion, character and duration of hypertension. The only notable difference between the two groups was age ($P < 0/001$).

Conclusion: CAD was diagnosed in 14 of 180 pheo pts (7.8%) and MI in 7 (3.9%). After pheo removal, post-infarction signs per ECG and ECHOCG remained only in two patients (1.1%). In most pheo patients, signs of CAD and MI were a result of coronary artery spasms and resolved after therapy with α-blockers and tumor removal.

Keywords: Pheochromocytoma; Hypertension; Coronary artery disease; Myocardial infarction