

5960 | BEDSIDE**Prevalence of prehypertension, hypertension and cardiovascular risk factors in a Belarus urban population**

V. Podpalov¹, A.I. Stchastlivenko¹, O.N. Zhurova¹, A.D. Deev², N.N. Ogrisko¹, V.G. Sorocina¹, V.V. Podpalov³, N.S. Balashenko¹, A.N. Barkovskiy¹, I.V. Belkina¹. ¹Vitebsk State Medical University, Vitebsk, Belarus; ²National Research Center for Preventive Medicine, Moscow, Russian Federation; ³Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus

Objective: To study the prevalence of prehypertension (preHT), hypertension (HT) and cardiovascular risk factors in a Belarusian Urban population.

Design and methods: We conducted a cross-sectional analysis of 3399 individuals (1884 men and 1545 women) living in a district of Vitebsk in January 2007. PreHT and HT were evaluated according to the JNC-7 (2003). The survey included standard questionnaires for detection of cardiovascular risk factors, measurements of blood pressure, electrocardiography, serum C-reactive protein and cholesterol data.

Results: Men and women were similar of mean age. During our study we received following data: preHT frequency was 34.3% (39.7% in men vs. 29.8% in women, $P < 0.001$); HT – 39.2% (40.3% in men vs. 38.6% in women, $P > 0.05$); overweight – 43.8% (43.2% in men vs. 44.3% in women, $P > 0.05$); family history of premature cardiovascular diseases – 29.9% (28.6% in men vs. 31.1% in women, $P > 0.05$); smoking – 41.8% (80.6% in men vs. 13.6% in women; $P < 0.001$); alcohol abuse – 18.7% (32.7% in men vs. 6.9% in women; $P < 0.001$), low physical activity – 31.9% (24.9% in men vs. 37.6% in women, $P < 0.001$); dyslipidemia – 64.1% (63.2% in men vs. 64.8% in women, $P > 0.05$). The preHT prevalence with adjustment age and sex was independently associated with following risk factors: body mass index ($P < 0.001$), family history of premature cardiovascular disease ($P < 0.001$), heart rate ($P < 0.001$), alcohol abuse ($P < 0.05$), smoking ($P < 0.1$). The HT prevalence with adjustment age and sex was independently associated with following risk factors: level of education ($P < 0.01$), body mass index ($P < 0.001$), family history of premature cardiovascular disease ($P < 0.001$), heart rate ($P < 0.001$), alcohol abuse ($P < 0.001$), smoking ($P < 0.001$), low physical activity ($P < 0.001$), total cholesterol ($P < 0.05$), LDL cholesterol ($P < 0.05$), triglycerides ($P < 0.05$).

Conclusions: The high prevalence of preHT, HT and cardiovascular risk factors is noted as men and women in a Belarusian Urban population.

5961 | BEDSIDE**Childhood determinants of blood pressure and prehypertension in adolescents - results from the SAPALDIA youth study**

J. Dratva¹, E.Z. Zemp¹, E.S. Schaffner¹, L.S. Saleh², R. Bettschart³, T. Rothe³, J.M.G. Gaspoz⁴, T. Rochat⁴, D.S. Stolz⁵, A. Turk⁵, C.S. Schindler¹, N.K. Kuenzli¹, N.P.H. Probst-Hensch¹ on behalf of SAPALDIA. ¹Swiss Tropical and Public Health Institute, Basel, ²University Institute for Clinical Chemistry, Zürich, ³Lungenpraxis/Pneumologie, Aarau, Davos, ⁴University Hospital of Geneva, Geneva, ⁵Pneumologie, University Basel/Falittberg Wald, Switzerland

Background: Hypertension has become the leading risk factor contributing to the global disability adjusted life years. Adolescent hypertension is increasing, possibly due to the obesity epidemic, and is known to track into adulthood. The SAPALDIA Youth Study, a nested study within the adult Swiss Air Pollution And Lung and Heart Disease In Adults cohort (SAPALDIA), aims to investigate early life factors and cardiovascular health in adolescents, with a special focus on active tobacco exposure.

Methods: 288 SAPALDIA offspring (mean age 15 years, sd 3.5) underwent clinical examination and reported on early life, health and lifestyle, smoking habits and disease history. Parental determinants and disease status were taken from the SAPALDIA adult cohort data. The mean of two blood pressure measurements, following standard protocols, was calculated for analyses. Prehypertension in childhood was defined as average systolic (SBP) or diastolic blood pressure (DBP) levels ≥ 90 th percentile but < 95 th percentile for gender, age, and height, respectively in adolescents $\geq 120/80$ mmHg (2). Descriptive and multi-level regression analyses were performed to investigate the independent impact of early life determinants on blood pressure and prehypertension.

Results: Prehypertensive values were found in 24%. We confirmed the impact of BMI on SBP (1 mmHg/10 percentile points, 95% CI 0.04, 0.14, DBP 0.02 mmHg, 95% CI -0.02; 0.06), and of high physical activity (≥ 60 min strenuous activity/day, SBP -3mmHg, 95% CI -6.0; 0.1, DBP -2.2 mmHg, -4.5; 0.1) and found a borderline significance for weekly smoking on SBP (SBP 3.6 mmHg; 95% CI -0.82; 8.0; DBP 2.3 mmHg, 95% CI -1.2; 5.7). Additional adjustment for parental education, smoking and cardiovascular risk strengthened the adverse association seen for weekly smoking. Associations with DBP proved less significant. Similar results were found in analyses with prehypertension.

Conclusion: A high percentage of youth presented with prehypertension. Considering the impact of modifiable risk factors, and the high risk of prehypertension turning into clinical hypertension, screening for prehypertension and risk factors in youth should be given full attention to reduce the population risk by optimal metabolic control and lifestyle modification.

Reference: 1. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics 2004

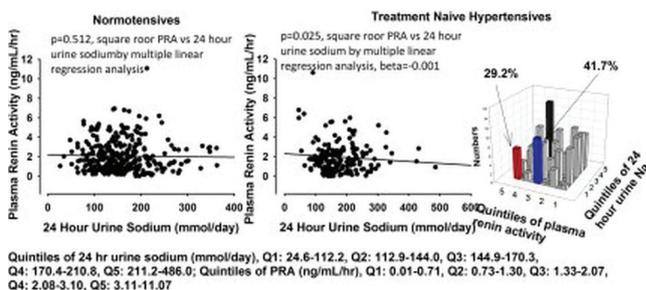
NOVEL INSIGHTS INTO THE RENIN-ANGIOTENSIN SYSTEM IN HYPERTENSION**5962 | BEDSIDE****Relationship between plasma renin activity and 24-hour urinary sodium excretion: low sodium intake is dangerous by elevation of renin?**

M.Y. Rhee¹, J.H. Kim¹, S.J. Shin¹, C.Y. Lim¹, S.W. Kim², D.Y. Nah³. ¹Dongguk University Ilsan Hospital, Goyang, Korea, Republic of; ²Dongguk University, Seoul, Korea, Republic of; ³Dongguk University College of Medicine Gyeongju Hospital, Gyeongju, Korea, Republic of

Backgrounds: Although sodium intake reduction lowers the development of hypertension and cardiovascular disease, previous studies reported the elevation of renin by short-term sodium reduction intervention.

Methods: Plasma renin activity (PRA) and 24-hour urine sodium (24HUNA) were measured from 529 individuals (mean age 47.3 \pm 9.5 year, men=207) in a community-based, cross-sectional study. Multiple linear regression analysis was adjusted with age, 24-hour systolic blood pressure, 24-hour heart rate, fasting blood glucose and gender. PRA of 24HUNA quintiles were compared by ANCOVA.

Results: Normotensive individuals (n=295, 44.8 \pm 9.9 years) showed no relationship between square root PRA and 24HUNA. Treatment naive hypertensive individuals (HT, n=164, 48.8 \pm 7.5 years) showed a significant correlation between square root PRA and 24HUNA by multiple linear regression analysis ($p=0.025$). The lowest quintile 24HUNA (≤ 112.2 mmol/day) of treatment naive HT had significantly higher PRA (2.87 \pm 2.38 ng/mL/hr) compared to other quintiles ($p=0.004$). However, 3rd quintile of PRA has the highest prevalence (41.7%, the highest PRA quintile=29.2%). The numbers of Individuals having > 4 ng/mL/hr of PRA were 4 of 24 (16.7%). HT taking antihypertensives (n=70, 54.1 \pm 7.5) had higher PRA compared to treatment naive HT (5.52 \pm 8.03 vs 1.96 \pm 1.59 ng/mL/hr, $p < .0001$). Individuals taking renin-angiotensin-aldosterone system inhibitors had the highest level of PRA (11.48 \pm 12.05 ng/mL/hr).



Conclusion: Low 24HUNA was related to the elevated PRA only in treatment naive HT. However, the present study indicates that it is difficult to suggest that the elevation of renin is caused by low sodium intake in usual life, and to extrapolate the elevation of renin in short-term intervention to long-term danger of sodium intake reduction.

5963 | BENCH**Number needed to treat and reduction of outcomes with RAAS inhibitors**

J.J. Mourad¹, J. Brugts², M. Bertrand³. ¹AP-HP - Hospital Avicenne - Paris 13 University, Bobigny, France; ²Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands; ³Lille Heart Institute, Lille, France

Incorporating the results of randomized trials into clinical practice is of high priority for physicians. In this regard, number needed to treat (NNT) has given decision makers access to a more intuitive statistical tool compared with relative risk reduction (RRR) in assessing treatment efficacy.

Objective: Mortality and cardiovascular (CV) events were compared in hypertension trials involving angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) based on NNTs to illustrate differences in CV protection of these two classes.

Design and objectives: All-cause and CV mortality as well as coronary and cerebrovascular events were analysed in a selection of 20 large randomized trials enrolling a total of 158 998 hypertensive patients as previously reported in a meta-analysis published by van Vark et al. in the European Heart Journal in 2012. NNT was calculated over the 4.3 years follow-up as the inverse of the absolute risk reduction between active treatment and comparator.

Results: Among renin-angiotensin-system antagonists, only ACE inhibitors significantly reduced all-cause mortality. Respectively 70 and 124 patients have to be treated with an ACE-inhibitor to prevent one all-cause and cardiovascular death. For ARBs, with the same objectives, respectively 446 and 750 patients have to be treated. The protective effect of ACE inhibitors is due more to coronary event reduction (NNT=54) than to cerebrovascular events reduction (NNT=1415). For ARBs the trend was opposite, showing a greater decrease in cerebrovas-

cular events (NNT=173) than in coronary events (NNT=3580). Among ACE inhibitor trials, the largest mortality reductions were observed in ASCOT-BPLA, ADVANCE, and HYVET which studied perindopril (RRR 13%, $P<0.001$), due to reduction in both coronary event reduction (NNT=109) and cerebrovascular events (NNT=131).

Conclusion: In hypertension trials, NNT analysis of morbidity and mortality provides relevant figures to compare the cardioprotective effect of treatments. This analysis confirms that coronary event reduction is an important component of mortality reduction observed with ACE inhibitors.

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Gender specific effects of valsartan on fibrinolysis in hypertensive patients with metabolic syndrome

M. Miyata, S. Hamasaki, C. Tei on behalf of KACT-Mets Investigators. *Kagoshima University, Department of Cardiovascular, Respiratory and Metabolic Medicine, Kagoshima, Japan*

Background: The purpose of this study was to analyze the effect of valsartan on a prothrombotic state in hypertensive patients with metabolic syndrome.

Methods and results: We conducted a multicenter, prospective, randomized, parallel-group controlled trial in 150 hypertensive patients with metabolic syndrome (87 men, 63 women). They were randomly assigned either to receive 80-160 mg valsartan per day (valsartan group, $n=79$) or to other conventional treatment without renin-angiotensin-system (RAS) inhibitor (non-RAS inhibitor group, $n=71$). After 1 year, there were no significant differences between the two groups in changes in systolic and diastolic blood pressure (valsartan: $153\pm 15/86\pm 15$ to $138\pm 16/77\pm 12$ mmHg; non-RAS inhibitor: $150\pm 14/82\pm 15$ to $137\pm 15/76\pm 10$ mmHg). There was a significant difference in the change of plasminogen activator inhibitor-1 (PAI-1) levels after 1 year between the two groups (valsartan: -3.7 ± 3.2 ng/mL; non-RAS inhibitor: 5.8 ± 3.3 ng/mL, $p=0.04$). In analysis of the gender difference, valsartan significantly reduced the PAI-1 levels compared to non-RAS treatment in postmenopausal women (valsartan: -5.7 ± 2.8 ng/mL; non-RAS inhibitor: 7.9 ± 3.9 ng/mL, $p=0.006$), but not in men (valsartan: -1.7 ± 5.5 ng/mL; non-RAS inhibitor: 4.7 ± 4.8 ng/mL, $p=0.38$).

Conclusions: Valsartan reduced plasma PAI-1 levels compared to non-RAS inhibitor in hypertensive patients with metabolic syndrome, and was suggested to be useful for the improvement of fibrinolytic function. In addition, this effect might be stronger in menopausal women compared to men.

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Changes in arterial stiffness after three years of treatment with ramipril or irbesartan in never treated patients with essential hypertension

H. Triantafyllidi, P. Triviliou, I. Ikonomidis, S. Tzortzis, K. Kotsas, G. Pavlidis, D. Kremastinos, M. Anastasiou-Nana, J. Lekakis. *University of Athens, Athens, Greece*

Purpose: Subclinical organ damage, an intermediate stage in the continuum of vascular disease, is an important determinant of cardiovascular risk. We aimed to study the long-term influence of ramipril or irbesartan treatment regarding arterial stiffness in never treated patients with essential hypertension.

Methods: We studied 122 non-diabetic, recently diagnosed and never-treated patients with essential hypertension (mean age 54 ± 11 years, 70 males). At baseline, we performed: a. 24h ambulatory blood pressure monitoring (ABPM) and b. carotid-femoral artery pulse wave velocity (PWV) using the Complior apparatus in order to evaluate arterial stiffness. After baseline evaluation, all patients randomized to treatment with ramipril or irbesartan targeting office blood pressure $<140/90$ mmHg. A second evaluation was performed three years later regarding office blood pressure (BP), ABPM and PWV. We characterized as well controlled patients those with 24h systolic and diastolic blood pressure $<135/85$ mmHg and as having normal arterial stiffness when PWV was <10 m/sec.

Results: Regarding total population, treatment with ramipril or irbesartan resulted to: a. office BP decrease (systolic BP 148 ± 16 vs. 134 ± 16 mmHg, $p<0.001$ and diastolic BP 90 ± 10 vs. 83 ± 8 mmHg, $p<0.001$), b. 24h BP decrease (systolic BP 140 ± 10 vs. 123 ± 14 mmHg, $p<0.001$ and diastolic BP 90 ± 9 vs. 75 ± 8 mmHg, $p<0.001$), and c. PWV increase (10.7 ± 2 vs. 11.2 ± 2 m/sec, $p<0.01$). 24h ambulatory BP was well controlled in 70% of the hypertensives (systolic BP 138 ± 9 vs. 120 ± 14 mmHg, $p<0.001$ and diastolic BP 89 ± 8 vs. 73 ± 6 mmHg, $p<0.001$). The two groups of controlled hypertensives under ramipril or irbesartan were matched for age, sex, BMI, office and 24h BP and baseline PWV. Regarding subgroups, PWV remained unchanged in the controlled hypertensives, the controlled hypertensives by irbesartan and the controlled hypertensives with baseline PWV >10 m/sec. However, PWV was significantly increased in uncontrolled hypertensives ($p<0.001$), the controlled hypertensives by ramipril ($p=0.01$) and the controlled hypertensives with baseline PWV <10 m/sec ($p<0.001$).

Conclusions: Long-term successful antihypertensive treatment resulted to inhibition of PWV increase only if patients received irbesartan instead of ramipril. Additionally, antihypertensive treatment manages to inhibit PWV increase in those patients with baseline arterial stiffness above normal limits.

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Effect of antihypertensive treatment with a combination of telmisartan and amlodipine on vascular structure and function

A. Jagodzinski¹, C. Goller², T. Zeller¹, D. Wachtlin³, S. Appelbaum¹, T. Muenzel², P. Wild², S. Blankenberg¹. ¹University Heart Center Hamburg, Clinic for General & Interventional Cardiology, Hamburg, Germany; ²University Medical Center of the Johannes Gutenberg University Mainz, Department of Medicine II, Mainz, Germany; ³Interdisciplinary Centre for Clinical Trials, University Medical Centre, Mainz, Germany

Purpose: Various antihypertensive combination therapies are available to treat arterial hypertension. Aim of the present study was to comparatively assess the effects of two usual combinations with an ARB, either combined with a thiazide diuretic or a CCB, on vascular function and structure phenotypes beyond blood pressure reduction.

Methods: The "Telmisartan and Amlodipine Study to Assess the Cardiovascular PROTECTive effects as measured by endothelial dysfunction (FMD) in hypertensive at risk patients beyond blood pressure" Study (TEAMSTA protect I Study) is a randomised, double blind, controlled, single centre study. Patients with controlled or uncontrolled hypertension were included in the trial receiving either the combination of either telmisartan and amlodipine (T/A) or olmesartan and hydrochlorothiazide (O/H) for 26 weeks. Primary endpoint was the change in flow mediated dilation (FMD) after 6 months compared to baseline examination. Secondary endpoints were the change of intermediate phenotypes of cardiovascular disease including structural and functional vascular parameters.

Results: Between August 2010 and 2011, 576 subjects (68% males) aged 35 to 82 years have been enrolled into the trial. Treatment groups were concordant concerning the cardiovascular risk profile. Blood pressure reduction was comparable in both treatment groups after 26 weeks (O/H -12 mmHg, T/A -13 mmHg; $p=0.805$). Both, T/A and O/H did not affect flow mediated dilation (FMD), the primary endpoint, in a post-hoc prevasodilation-adjusted calculation. However, T/A reduced the Augmentation Index (AI) measured by digital volume plethysmography and ultrasound-based Intima Media thickness, whereas O/H had no effect (T/A vs O/H: DAI, p for difference=0.025; DIMT, p for difference=0.011). Stiffness Index by digital photoplethysmography was reduced in the T/A group (D -0.868 m/s, $P=0.000$); however, there was no difference between treatment groups ($p=0.104$) as well as NTproBNP was significantly reduced in the T/A group (DT/A $p=0.002$, D O/H $p=0.055$; p for difference = 0.447).

Conclusion: Both combination therapies reduced blood pressure effectively and without observed differences between the treatment groups. Although the trial failed to show effects on endothelial function of the brachial artery after 6 months, T/A seems to have beneficial effects on arterial stiffness beyond blood pressure lowering which suggests additive cardioprotective effects. Further efforts are needed to elucidate the biological mechanisms of these findings and the impact on the outcome.

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The velocity of antihypertensive effect of candesartan/hydrochlorothiazide combination and incremental dose of candesartan evaluated by daily serial morning home blood pressure measurements

M. Hosaka¹, K. Asayama², H. Metoki³, M. Satoh¹, T. Obara³, M. Kikuya³, T. Ohkubo⁴, Y. Imai¹ on behalf of for the J-HOME-CARD Study Group. ¹Tohoku University Graduate School of Pharmaceutical Sciences, Sendai, Japan; ²Catholic University of Leuven, Department of Cardiovascular Diseases, Leuven, Belgium; ³Tohoku University Graduate School of Medicine, Sendai, Japan; ⁴Shiga University of Medical Science, Shiga, Japan

Purpose: The hypotensive effect and the time to attain the maximum antihypertensive effect (stabilization time) of candesartan 8mg/ hydrochlorothiazide 6.25 mg combination therapy (combination group) and therapy with a 12 mg of candesartan (increment group) were compared by analysing exponential decay functions using daily serial morning home blood pressure (BP) measurements.

Methods: In this multicentre Japan Home versus Office BP Measurement Evaluation with Candesartan and Restricted dose of Diuretic (J-HOME-CARD) study, we enrolled essential hypertensive patients treated with low-dose candesartan (8 mg) for ≥ 4 weeks, in whom a target morning home systolic BP (SBP), 135 mmHg, was not achieved. They were randomised into the combination group ($n=103$) and the increment group ($n=103$).

Results: The combination therapy provided additional reduction of 3.4mmHg

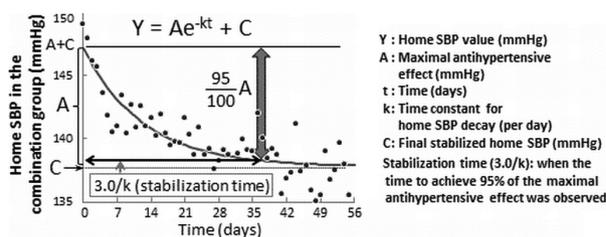


Figure 1