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PS08/MON/18 – Association of the -344T/C polymorphism of CYP11B2 aldosterone synthase gene with essential hypertension in Czech population

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Objectives: Renin-angiotensin-aldosterone system is an important regulator of the blood pressure (BP). Molecular variants in genes that encode components of this system could be associated with several cardiovascular diseases, such as essential hypertension. Among them the aldosterone synthase gene (CYP11B2) represents an important candidate gene region for BP regulation and cardiac hypertrophy. We therefore studied the association of -344T/C polymorphism of the CYP11B2 gene with the presence and severity of essential hypertension in Caucasian population of Czech Republic. **Methods:** We genotyped 213 hypertensive patients (122 controlled hypertensives, 73 hypertensives resistant to the triple antihypertensive therapy) and 156 normotensive subjects for the -344T/C polymorphism using polymerase chain reaction-restriction fragment length polymorphism analysis. **Results:** The distribution of genotypes in normotensive controls and essential hypertensive subjects were: TT 25.6% vs. 31.9%, TC 51.9% vs. 57.3% and CC 22.4% vs. 10.8%. The -344T/C variant was associated with hypertension. Hypertensive patients had significantly higher frequency of T allele and lower frequency of C allele ($\chi 2=5.89$, $p<0.05$) and CC genotype ($\chi 2=9.44$, $p<0.01$) compared to normotensive group. We did not observe an association of -344T/C variant with the resistance of hypertensive patients to the antihypertensive combination therapy. **Conclusion:** Our case-control study indicates an association of -344T/C polymorphism of aldosterone synthase gene with a genetic predisposition to the development of essential hypertension in Czech population and supports a potential role of this polymorphism in BP regulation. Study was supported by the research project of the Ministry of Health of Czech Republic (MZO 00064165).

PS08/MON/19 – Telomere attrition rate in a longitudinal population study

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Objectives: Cardiovascular disease is associated with reduced telomere length of replicating somatic cells. Most epidemiological studies do not have repeated DNA samples to chart in a longitudinal way each individual's telomere attrition rate. We measured the rate of telomere attrition and its determinants in a longitudinal population study and to compare cross-sectional with longitudinal estimates of the telomere attrition rate. **Methods:** In 143 randomly selected participants (mean age, 48.4 years; 52.4% women) from the FLEMENGHO study, we measured leukocyte telomere length, as expressed by mean terminal restriction fragment (TRF) length, at baseline and after 7.5 years (median) of follow-up (interquartile range: 7.3 to 8.2 years). **Results:** Age was a significant determinant of TRF length at baseline and follow-up ($p<0.0001$), accounting for 15.8% and 18.4% of the variance, respectively. In the cross-sectional analysis of the baseline and follow-up data, the estimates of TRF length shortening per year were 0.022 kb (95%CI: -0.031 to -0.014) and 0.021 kb per year (95%CI: -0.028 to -0.014), respectively. In the longitudinal analysis, the measured TRF length attrition rate per year averaged -0.017±0.79 kb per year (95%CI -0.16 to 0.098). The main determinants of TRF length at follow-up explaining 60.1% of the variance, were TRF length at baseline (partial regression coefficient, 0.59±0.050; $p<0.0001$) and HDL cholesterol at baseline (0.261±0.089; $p=0.004$). Telomere attrition rate correlated with averaged telomere length (-0.0349±0.0087 kb/year; $p<0.0001$) and HDL cholesterol at baseline (0.037±0.015 kb/year; $p=0.01$). **Conclusion:** Shortening of telomeres is less prominent in subjects who already have a short TRF length and in those with higher HDL-cholesterol. Our study for the first time validated cross-sectional estimates of the TRF length attrition rate against longitudinal measurements.

PS08/MON/20 – Familial elevation of serum angiotensin-converting enzyme (ACE) due to a new splice site mutation of the ACE gene

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Background: Serum angiotensin-converting enzyme (sACE) is classically increased in systemic granulomatous disorders such as sarcoidosis as well as in Gaucher's disease, leprosy and hyperthyroidism. Several cases of familial elevation of sACE have also been described. In particula lies studied by Kramers et al. (Circulation 2001;104:123(cosegregated with a mutation in the stalk of the enzym new pedigree with striking sACE elevation associated wi the ACE gene. **Results:** A 41-year-old woman was ad of a fortuitously discovered increase in sACE (146 IU/l otherwise asymptomatic patient. She was normotensive (had no left ventricular hypertrophy or overt cardiovascu examination was unremarkable. A comprehensive work out systemic disorders associated with sACE increase. A sACE was then suspected. Serum ACE levels were deter of the index patient (median age: 44 year-old, range: 2 a 5-fold increase in sACE level was found in 6 out of analysis of the ACE gene disclosed a new heterozygous of intron 25, consistently associated with increased sACE IU/l in subjects harbouring the mutation vs. 12.4 and wild-type subjects). All siblings were normotensive and hypothesize that the splice site mutation leads to skippin encodes the transmembrane domain of ACE, and thus to large amounts of the soluble form of the enzyme. **Conclu** new splice site mutation of the ACE gene associated with in sACE, apparently without hypertension or cardiova Increased sACE levels are not necessarily synonymous disease, and familial elevation should be considered.

PS08/MON/21 – Repeated replication and a prosp meta-analysis of the association between chromosom coronary artery disease

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Background: Recently, genome-wide association studies on chromosome 9p21.3 to affect the risk of coronary art We investigated the association of this locus with CA control studies and undertook a meta-analysis. **Methods:** polymorphism, rs1333049, representing the 9p21.3 locus seven case-control studies involving a total of 4,645 patie infarction (MI) or CAD and 5,177 controls. The mode determined. A meta-analysis of the present data and pu samples was conducted. A limited fine-mapping of the loc **Results:** The risk allele (C) of the lead SNP rs13330 associated with CAD in each study ($p < 0.05$). In a pooled ratio per copy of the risk allele was 1.29 (95% CI: [1.22 An autosomal additive mode of inheritance best explain association. The meta-analysis of the rs1333049 SNP in 28,949 controls increased the overall level of evidence fo CAD to $p = 6.04\times10^{-10}$ (OR 1.24 [1.20, 1.29]). Genotypi SNPs in the region identified several with highly significa CAD but none had predictive information beyond that SNP. **Conclusion:** This broad replication provides unpreced association between genetic variants at chromosome 9p21.

PS08/MON/22 – MTHFR gene variants and essenti Common single nucleotide polymorphisms in Asian I essential hypertension

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Objectives: Polymorphisms in the methylenetetrahydrofola are known to be associated with hyperhomocysteinemia (the extent of genetic influence on plasma homocysteine (H for essential hypertension (EH) remains uncertainMany a have investigated common polymorphisms (MTHFR C67 their role in HHcy and hypertension with inconsistent resu based approach has been found to be superior in explai interaction. The aim of present study was to examine th four known polymorphisms of MTHFR gene (C677T, A12 T1317C) and their haplotypes with Hcy and EH. **Method** a prospective case-control study involving 280 EH patients controls of North Indian origin. Genotyping was performe Chain Reaction-Restriction Fragment Length Polymorphi and plasma Hcy and folate levels were measured. **Results:** H were significantly higher and folate levels were lower in pati to controls ($p<0.05$). The frequency of mutant 677CT, 1298 genotypes were higher in patients, and were associated wi levels and increased risk of hypertension ($p<0.05$). Two hapl (with 1298C and 1793A mutant alleles) and T-A-G-T (wi allele) were associated with increased risk of EH (3.5 fold individual genotypes. **Conclusion:** A haplotype-based appro