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### **P4.59: ASSOCIATION BETWEEN ENDOTHELIAL NO SYNTHASE POLYMORPHISM AND AORTIC STIFFNESS**

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subjects aged 71±6 yrs (mean±SD) from an existing community study. Incremental LV elastances at the start ( $E_{se}$ ) and end of ejection ( $E_{ee}$ ) were calculated as the ratio of  $dp/dt$  and  $dV/dt$  at corresponding positions in time. In our analysis we considered the inter-relationships of  $E_{ee}$  with heart rate (HR), systolic blood pressure (SBP), pressure relaxation rate ( $dp/dt_{ee}$ ), arterial compliance ( $SV/PP$ ), mitral annulus velocity  $e'$ ,  $E/e'$ , ejection fraction (EF) and the classic non-invasive ventricular-vascular coupling index ( $Ees/Ea$ ). Univariate correlations (Table) as well as stratification according to lower and higher  $E_{ee}$  groups showed that a higher  $E_{ee}$  was associated with a higher  $E_{se}$  and with lower arterial compliance and reduced ventricular relaxation rate ( $e'$ ), despite increased  $dp/dt_{ee}$ . EF and  $Ees/Ea$  were not associated with any of these measures.

**Conclusions:** An increased  $E_{ee}$  reflects slowed ventricular relaxation, which may be due to the impact of reduced arterial compliance on LV diastolic performance. The classic non-invasive ventricular-vascular coupling index  $Ees/Ea$  did not reveal such a relationship.

**P4.57**  
**STIFFNESS OF THE LARGE ARTERIES IN INDIVIDUALS WITH AND WITHOUT DOWN SYNDROME**

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**Background:** Down syndrome (DS) is known to cause premature aging in several organ systems<sup>1</sup>. In this controlled study, the possibility of changes in the large arteries due to aging was evaluated in patients with DS<sup>1</sup>.

**Methods:** Eighty-two subjects of both genders were selected. The DS group had 41 active subjects. The control group was consisted of 41 healthy matched for age and gender. Carotid–femoral pulse wave velocity was obtained as an index of aortic stiffness using an automatic noninvasive method<sup>2</sup>.

**Results:** The general characteristics of the groups and the main results are shown in Table 1 and Figure.

**Conclusion:** Despite evidence in the literature that patients with DS undergo early aging<sup>1</sup>, this process does not seem to affect the large arterial trunks<sup>3</sup>. Considering that DS presents with chronic hypotension, it is reasonable to propose that the prolonged reduction of arterial distending pressure may contribute to functional preservation of the arteries in patients with Down syndrome

**Keywords:** aging, Down syndrome, pulse wave velocity, arterial stiffness

**References**

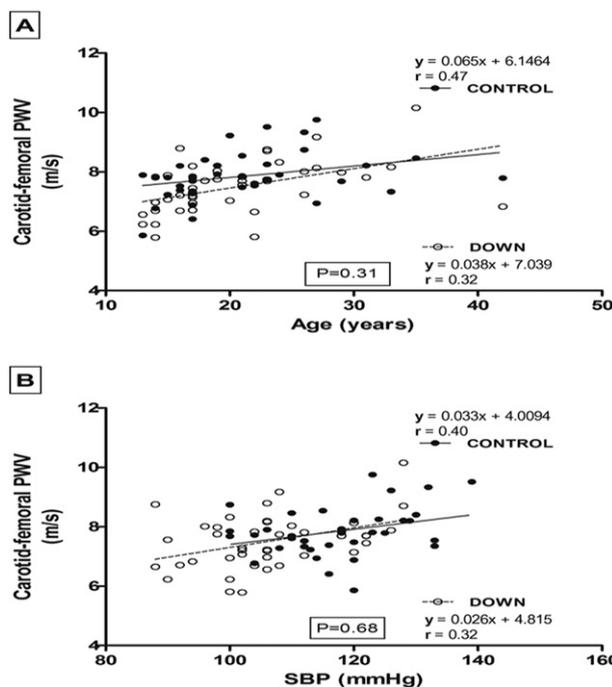
- 1 Nakamura E, Tanaka S. Biological ages of adult men and women with Down's syndrome and its changes with aging. *Mech Ageing Dev.* 1998; 105:89–103.
- 2 Asmar R, Benetos A, Topouchian J, et al. Assessment of arterial distensibility by automatic pulse wave velocity measurement. *Hypertension.* 1995; 26:485–490.

**Table 1** Anthropometric and hemodynamic characteristics in the experimental groups.

	DOWN SYNDROME (n=41)	CONTROL (n=41)	P value
Age (years)	21 ± 1	21 ± 1	-
Variance	(13-42)	(13-42)	
Weight (kg)	55 ± 2	61 ± 2	< 0.05
Height (m)	1.47 ± 0.01	1.64 ± 0.01	< 0.001
BMI (kg.m <sup>-2</sup> )	25 ± 1	22 ± 1	< 0.01
WHR	0.88 ± 0.01	0.80 ± 0.01	< 0.001
SBP (mmHg)	106 ± 2	117 ± 2	< 0.001
DBP (mmHg)	66 ± 2	77 ± 2	< 0.001
MAP (mmHg)	80 ± 1	90 ± 1	< 0.001
HR (bpm)	74 ± 2	76 ± 2	NS
PWV (m/s)	7.51 ± 0.14	7.84 ± 0.12	< 0.05

Data are expressed as mean ± standard error (SEM).

**Abbreviations:** DS = Down syndrome; BMI = body mass index; WHR = waist-hip ratio; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; HR = heart rate; PWV = pulse wave velocity; NS = not significant.



**Figure 1** Multivariate linear regression model with Pearson's correlation coefficient between age, systolic blood pressure, and carotid–femoral pulse wave velocity in controls and subjects with Down syndrome.

3 Rodrigues AN, Coelho LC, Gonçalves WLS, et al. Stiffness of the large arteries in individuals with and without Down syndrome. *Vascular Health and Risk Management* 2011; 7: 375–381

**P4.59**  
**ASSOCIATION BETWEEN ENDOTHELIAL NO SYNTHASE POLYMORPHISM AND AORTIC STIFFNESS**

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**Background:** Recently, rs3918226 polymorphism in the promoter region of endothelial NO synthase (NOS3) was strongly associated with arterial hypertension in a large genome-wide association study\*. We investigated whether this polymorphism is associated with arterial phenotypes in a Czech general population.

**Methods:** In a pilot study, we genotyped 101 untreated subjects (age, 54.0 years; 51.5% women, 30.7% smokers). Arterial properties were measured using SphygmoCor. In multivariate-adjusted analyses, we assessed effect of rs3918226 on aortic pulse wave velocity (aPWV) and augmentation index (AIx). As independent covariates we considered sex, age, MAP, heart rate and smoking.

**Results:** Frequency of rs3918226 genotypes were CC 85.2%, CT 14.8%, and TT 0%. Carriers of mutated T allele tended to have higher both aPWV (8.59±0.45 vs. 7.77±0.18 m/s; P=0.098) and AIx (91.77±3.56 vs. 85.89±1.45%; P=0.13) compared to CC homozygotes. These associations were modified by smoking. In smokers we observed similar trend as in the whole population (0.067<P<0.19), while in nonsmokers we did not find any association (P≥0.50). We did not observe any association between blood pressure and the polymorphism under study (P≥0.67).

**Conclusion:** This is first study to explore the association of rs3918226 polymorphism in NOS3 gene with arterial properties. We found marginally higher aPWV and AIx in carriers of mutated T allele in this pilot study. We hypothesize that genetic modulation of intermediate arterial phenotypes might lead to higher blood pressure. As the prevalence of

T allele is low, further study with sufficient number of subjects is warranted.

\* Salvi E et al., Hypertension 2012; 59: 248.

**P4.60**  
**DEFECT VENOUS WALL PROPERTIES AS WELL AS ARTERIOLAR REGULATION IN PATIENTS WITH VASOVAGAL SYNCOPE**

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The initiating trigger in vasovagal syncope (VVS) is unclear but impaired venous return has been considered as a central factor. A greater leg venous compliance (Vc) may augment the central hypovolemia during standing. The aim of the study was to evaluate Vc in VVS patients and controls.

15 VVS females (24.8±4.9 years) and 15 age-matched female controls (22.9±3.2 years) were studied. Venous occlusion plethysmography was used to measure calf volume changes. A thigh cuff was inflated to 60 mmHg for 8 min with a subsequent linear decrease of 1 mmHg/s in cuff pressure (P). Vc was determined using the first derivative of a quadratic regression equation describing the volume-pressure relationship [Compliance =  $\beta_1 + 2\beta_2(P)$ ]. The capillary filtration was subtracted from the volume curve to correct for the effect on Vc.

Vc was reduced in VVS females (P<0.05). No differences were found in the venous capacitance response or capillary filtration. Resting arterial blood flow was lower and the peripheral resistance higher in VVS females (P<0.05). The time for 50% of the capacitance response to be developed was increased in VVS females (P<0.05), and the rate of the capacitance response correlated to the reduced arterial inflow of blood (r=0.64, P<0.01).

The study shows defects both in venous wall properties and arteriolar regulation in patients with VVS. A reduced blood flow to the lower limb with a concomitant reduction in filling rate of the capacitance vessels during standing might change the central baroreceptor response with a defect hemodynamic adjustment as a consequence.

**P4.61**  
**ASSOCIATION BETWEEN ENDOTHELIUM-DEPENDENT VASODILATATION AND SERUM PULMONARY SURFACTANT PROTEIN D CONCENTRATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

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Pulmonary surfactant protein D (SP-D) is considered as a candidate biomarker for the functional integrity of the lung and for disease progression, which can be detected in serum. SP-D may function to modulate inflammation and host defense in the vasculature, which may impact the development or progression of cardiovascular disease. Circulating SP-D is supposed to be a predictor of cardiovascular morbidity and mortality and adding prognostic information to well-established risk factors.

**Aims:** measurement and assessment of serum SP-D level and endothelium-dependent vasodilatation in patients with chronic obstructive pulmonary disease (COPD).

**Methods and Results:** in 39 patients with II and III stage of COPD we have measured serum SP-D level and endothelium-dependent vasodilatation during reactive hyperemia test. Comparing II to III stage more impaired endothelium-dependent vasodilatation during reactive hyperemia test and reduced increase in brachial artery diameter in III stage were registered (median D 26% vs. D 10,9%, correlation -0,71, p<0,05). SP-D level also correlated with COPD stage (correlation 0,75, p=0,01). However, we didn't find reliable correlation between SP-D level and endothelium-dependent vasodilatation. At the same time endothelium-dependent vasodilatation has shown high correlation with serum pro-inflammatory and anti-inflammatory cytokines level, negative and positive, accordingly.

**Conclusion:** both worsening of endothelium function and SP-D concentration strongly correlates with stage of COPD. However, can suppose that endothelium dysfunction in COPD-patients isn't associated with SP-D serum concentration, and SP-D can't be assessed as the significant risk factor of endothelial dysfunction. This fact requires further investigation.

**P4.62**  
**PROGNOSTIC VALUE OF ARTERIAL STIFFNESS INDICES IN PATIENTS WITH ACUTE ISCHEMIC STROKE**

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It is unclear whether arterial stiffness predicts the outcome of patients with acute ischemic stroke. We aimed to assess the prognostic value of arterial stiffness in this population. We studied 280 consecutive patients (37.5% males, age 78.8±6.4 years) who were hospitalized in our Department for acute ischemic stroke between September 2010 and May 2012. Arterial stiffness was assessed by measuring the augmentation index (Alx), central systolic blood pressure (cSBP) and central pulse pressure (cPP) over the radial artery with the Sphygmocor device. The severity of stroke was assessed with the National Institute of Health stroke scale (NIHSS) score at admission and the outcome was assessed with the modified Rankin scale score at exit from the hospital. None of the indices of arterial stiffness correlated with NIHSS score at admission. Alx showed a negative correlation with the modified Rankin scale score at exit from the hospital (r=-0.200, p<0.05). cSBP and cPP correlated with the number of days of hospitalization (r=0.180, p<0.05 and r=0.225, p<0.05, respectively). Twenty-five patients (8.9%) died during hospitalization. These patients had lower Alx than patients who were discharged (18.2±11.3 vs. 29.9±9.8, respectively; p<0.005). Other indices of aortic stiffness did not differ between patients who died during hospitalization and those who were discharged. In conclusion, a higher Alx was associated with better functional outcome and lower mortality rate in patients with acute ischemic stroke. Competing causes of death and the relatively beneficial effect of elevated BP during the acute phase of stroke might partly explain this apparently paradoxical finding.