P4.04: BARORECEPTOR SENSITIVITY IS REVERSED IN DIABETES AND IS UNAFFECTED BY ANTI-HYPERTENSIVE TREATMENT: A RODENT STUDY

Z. Kouchaki, E. Salum, J. Kals, P. Kampus, A.P. Avolio, M. Butlin

P4.02
BASELINE CRP BUT NOT NSAID-USE PREDICTS FUTURE INCREASED ARTERIAL STIFFNESS IN ANKYLOSING SPONDYLITIS: RESULTS AFTER 5-YEAR FOLLOW UP

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Objective: Patients with ankylosing spondylitis (AS) have an increased risk of CVD, but previous studies have not shown a worsened risk profile regarding traditional cardiovascular risk factors. The objective was to investigate whether baseline CRP predicts future increased central arterial stiffness.

Methods: 5-year follow-up study of hospital recruited AS patients, with examinations in 2003 and 2008-2009. Information on demographics, co-morbidities and medication was assessed from questionnaires. Baseline CRP was measured in 2003. Arterial stiffness, measured as Augmentation index (AIx), was recorded in 2008-2009 (Sphygmocor apparatus, At Cor). Statistical analyses were performed using SPSS 20. Univariate associations between AIx and baseline predictors (education, smoking habits, BMI, use of NSAID and disease modifying anti-rheumatic drugs (DMARD), CRP) and factors known to have an effect on AIx (Central mean arterial pressure (CMAP), height, use of statins and antihypertensives) were adjusted for age and gender. Variables with a p-value<0.2 were included in a multivariate model. Non-significant variables were removed stepwise until only significant variables remained.

Results: 85 AS patients participated in this study. Baseline mean (SD) age was 47.3 (12.6) years. 59% were male, 25% smokers. Median (IQR) CRP (mg/l) 4 (2-13). In the multivariate linear regression models CRP was independently associated with higher future AIx (table).

Conclusion: Elevated CRP but not NSAID-use predicted higher future AIx, indicating that inflammation is a risk factor of CVD in AS.

Variables	Univariate beta (95% CI)	p-value	Multivariate beta (95% CI)	p-value
Age (years)*	0.7 (0.5-0.9)	<0.001	0.5 (0.3-0.7)	<0.001
Gender, male*	-12.0 (-17.3−-6.7)	<0.001	-10.9 (-14.4−-7.5)	<0.001
Education>12 years	-1.0 (-5.3-3.3)*	0.63		
Baseline predictors 2003				
Current smoking	3.9 (-0.5 -8.3)*	0.08		
BMI (m²/kg)	0.8 (0.0-1.6)*	0.04		
NSAID	2.7 (-2.5-7.8)*	0.30		
DMARD	-3.2 (-8.3-1.9)*	0.22		
CRP (mg/l)	0.2 (-0.0-0.3)*	0.06	0.2 (0.0-0.3)	0.02
Current factors 2008				
Height (cm)	-0.3 (-0.5−0.0)*	0.03		
CMAP (mmHg)	0.3 (0.1-0.5)*	<0.001	0.3 (0.1-0.4)	<0.001
Statins	6.2 (0.9-11.6)*	0.02	6.3 (1.5-11.2)	0.01
Antihypertensives	0.8 (-3.9-5.5)*	0.74		

*Adjusted age and gender

P4.03
APOPTOSIS IN THE MEDIA OF THE AORTIC WALL AND ITS RELATIONSHIP WITH AORTIC VALVE MORPHOLOGY IN AORTIC DILATATION

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Background: The aortic valve is normally tricuspid but may vary in that it can be made up of 1, 2 or 4 leaflets with each of these often associated with aortopathy, most commonly aortic dilatation. In patients with a bicuspid valve this association has been explained in part by molecular changes taking place in the smooth muscle cells of the aortic media resulting in their apoptosis.

Objectives: To investigate changes in apoptosis and their genetic regulators that occur in the aortic media of patients with aortic dilatation and whether this differs with different aortic valve configurations.

Methods: Aortic wall samples were collected from patients with unicuspid, bicuspid, tricuspid and quadricuspid aortic valve morphology. Samples underwent homogenisation and were then analysed for a number of apoptotic markers and their genetic regulators using western blot and rt-PCR.

Results: Cleaved caspase 3 expression is increased in the aortic media of both the unicuspid (1.1 μm^2) and bicuspid (0.42 μm^2) aortic valve samples as compared to the tricuspid (0.060 μm^2) sample. Relative gene expression of P53:BCL-X$_L$ >1 in the aortic media of unicuspid and bicuspid aortic valves whilst p53:BCL-X$_L$<1 in the media of the tricuspid sample.

Conclusion: Cleaved caspase 3 assay demonstrates that smooth muscle cell apoptosis is increased in the dilated aortic media of unicuspid and bicuspid aortic valves as compared to that of the tricuspid aortic valve. This increase in apoptosis is mediated by an increase in the ratio of proapoptotic p53 to antiapoptotic BCL-X$_L$ and may explain the association between abnormal valve morphology and aortic dilatation.

P4.04
### BARORECEPTOR SENSITIVITY IS REVERSED IN DIABETES AND IS UNAFFECTED BY ANTI-HYPERTENSIVE TREATMENT: A RODENT STUDY

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Objectives: Diabetes is a complex disease associated with cardiovascular complications. This study compared baroreceptor sensitivity (BRS) in diabetic rats with and without anti-hypertensive treatment.

Methods: Diabetes (induced by intraperitoneal injection of streptozotocin at 6 weeks of age) and control (saline injection) rats were divided into untreated (diabetic n=9, control n=5) and treated (diabetes+Tx n=9, control+Tx n=6) groups. Treatment groups received angiotensin II receptor antagonist, telmisartan (10 mg/kg/day, gavage). At 17 weeks of age, systolic pressure was measured by tail-cuff technique. The following week, rats were anaesthetised (urethane, 1.3 g/kg) and aortic pressure and heart rate measured during intravenous phenylephrine infusion (30 μg/kg/min). BRS was calculated by the slope of heart rate against mean pressure rise. Normal BRS was defined as a positive slope, and BRS dysfunction as a negative slope (Figure).

Results: Both control (142$\pm$16 mmHg) and diabetic (132$\pm$22 mmHg) animals were hypertensive. Anti-hypertensive treatment successfully lowered systolic blood pressure (control+Tx 105$\pm$11 mmHg; diabetes+Tx 119$\pm$14 mmHg). BRS was typically positive in control (100%) and control+Tx (83%) rats. Conversely, BRS was impaired in both diabetic (33% positive) and diabetes+Tx (29% positive) rats. BRS impairment was significantly different between diabetic and control rats (p=0.007) and diabetes+Tx and control+Tx rats (p=0.002). However, there was no difference with anti-hypertensive treatment (diabetes, diabetes+Tx: p=0.42; control, contol+Tx: p=0.32).

Conclusion: Baroreceptor sensitivity is impaired in diabetic rats and this is independent of the hypertensive state.

normal BRS function (control and control +Tx) — BRS dysfunction (diabetes and diabetes+Tx)
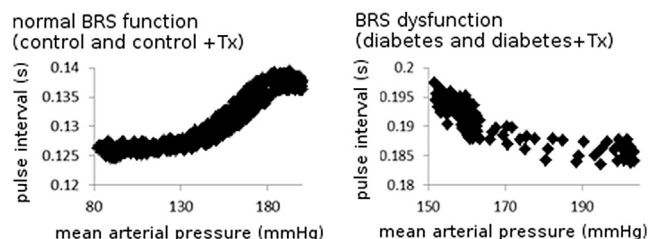
P4.05
POLYCYSTIN DEFICIENCY RESULTS IN COMPLETE LOSS OF NO SYNTHESIS DURING SUSTAINED FLOW-MEDIATED DILATATION OF CONDUIT ARTERIES IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: POSSIBLE REVERSAL BY DOPAMINE

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