P1.56: DETERMINANTS OF AORTIC STIFFENING IN DIABETES: THE INFLUENCE OF COLLAGEN TURNOVER, AUTONOMIC DYSFUNCTION, AND SYSTEMIC INFLAMMATION

S. Bunce, A. Stride, C. Matthews, W.D. Fraser, J.C. Smith

Methods: 132 normotensives (83 males, mean age 40.6 years) were divided in group A: non/light smokers (<5 pack-years, 67 subjects) and group B: heavy smokers (≥5 pack-years, 65 subjects). Augmentation index (AI) was measured using a validated device The A-to-G substitution was typed by BbvI digestion of specific PCR products amplified from DNA.

Results: The two groups did not differ regarding sex, peripheral pressures, BMI and lipids (p=NS). Group A had lower AI than group B (16.5±12.5% vs 23.1±12.2%, p<0.01). In group A, the prevalence of AA vs AG+GG genotypes was 19.4% and 80.6; when compared to AA subjects, AG+GG subjects demonstrated higher levels of AI (AA:8.7±6.2% vs AG+GG: 18.4±13%; p=0.01). In group B, the prevalence of AA vs AG+GG was 29.2% and 70.8%; AI levels did not vary between the two subgroups (AA:24.3±11.3% vs AG+GG: 22.6±12.6%; p=NS).

Conclusion: In non/light smokers presence of the G allele accounts for deteriorated arterial elastic properties. This is not the case in heavy smokers, as wave reflections are equally impaired irrespectively of the G allele presence. These findings underscore the need for further research into the interplay between intrinsic, extrinsic oxidative stress and arterial function.

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P1.54
THE RELATIONSHIP OF THE INSULIN-LIKE GROWTH FACTOR (IGF) SYSTEM TO CARDIOVASCULAR STRUCTURE AND FUNCTION IN WOMEN

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Introduction: IGF-I and its binding proteins (BP) may modulate cardiovascular risk, from young ages. We examined relationships of IGF system indices (IGF-I, -BP-1, BP-3, IGF-I/BP-3 ratio) to cardiac and vascular structure & function across the whole vascular bed.

Methods: 193 women in our Manchester Mothers' Cardiovascular (CVS) study followed from an index pregnancy aged 32±5y had fasting blood samples, anthropometry, echocardiography, aortic pulse wave velocity and heat augmented laser doppler flowmetry (LDF). In a smaller subgroup (n=29), subcutaneous small artery structure and function was assessed *ex-vivo* by wire myography. IGF-I and IGFBP-3 were assayed by Elisa, and IGFBP-1 by radio-immunoassay.

Results: On multiple regression analysis, adjusting for age, ethnicity, smoking history, BMI, systolic blood pressure, fasting glucose, total cholesterol and triglycerides, IGF-I, IGFBP1 and the IGF-I/BP-3 ratio were independently related to CVS parameters as follows:

CVS parameter	IGF system	Beta	95% CI of Beta	p
LV Posterior Wall thickness	IGF-I/BP-3 ratio	−0.005	-0.009 to 0.00	0.04
Proximal aortic distensibility (echo)	IGF-I/BP-3 ratio	−0.014	-0.028 to 0.00	0.05
Heat augmented microcirculatory flow (LDF)	IGF-I/BP-3 ratio	0.05	0.007 to 0.094	0.03
	Ln IGFBP1	−0.66	-1.09 to -0.22	0.004
Subcutaneous small artery media: lumen ratio(n=29)	Total IGF-I	0.19	0.07 to 0.31	0.003
	IGF-I/BP-3 ratio	2.09	1.54 to 2.63	<0.001
	Ln IGFBP1	−28.0	-44.85 to -11.17	0.002

Conclusion: In relatively young women, higher concentrations of IGF-I, 'free' IGF-I (= IGF-I/BP-3 ratio) and of IGFBP-1 had marked influences on cardiac, large and small vessel structure and function.

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P1.55
INFLUENCE OF THE SOLUBLE CD14 ON AORTIC STIFFNESS USING A MENDELIAN RANDOMIZATION

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Background: CD14 receptor is at the crossroads between infection and inflammation. Present on the myeloid cell surface, it binds lipopolysaccharides and induces a release of cytokines whose deleterious effects on the arterial wall have been documented. Present as soluble protein (sCD14), its blood concentration increases in response to bacterial invasion and partly inhibits response to lipopolysaccharide of macrophages. In humans, soluble CD14 has been associated with aortic stfffness.

Objective: The aim of this study was to analyse in a large population-based sample the relationship of sCD14 with aortic stiffness using a Mendelian randomization approach.

Methods: 1015 subjects randomly selected from the polling lists, were recruited by the Toulouse MONICA center. After fasting, blood sample was drawn, blood pressure and carotid femoral pulse wave velocity were successively measured in supine position. sCD14 was measured using an immunoenzymatic method. A genotypic examination for the CD14 C260T polymorphism was performed.

Results: An increase in sCD14 expression was observed in subjects carrying t allele (p<0.001). No significant difference in intima-media thickness, number of plaques and pulse wave velocity was noticed according to C260T polymorphism. An interaction was observed between C260T polymorphism and current smoking in sCD14 expression: among smokers, no significant change in sCD14 was observed in individuals carrying t allele.

*adjusted for age and risk factors	CC	CT	TT	p	p*
	N=218	N=433	N=235		
sCD14 (mg/ml)	3.36 ± 1.02	3.56 ± 1.06	3.66 ± 0.97	0.008	0.003
PWV m/s	8.95 ± 1.65	8.96 ± 1.73	9.01 ± 1.71	0.45	-

Conclusion: This large population—based study does not support the causative nature of the link observed between soluble CD14 and aortic stiffness.

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P1.56
DETERMINANTS OF AORTIC STIFFENING IN DIABETES: THE INFLUENCE OF COLLAGEN TURNOVER, AUTONOMIC DYSFUNCTION, AND SYSTEMIC INFLAMMATION

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Although aortic stiffening is a strong predictor of cardiovascular mortality in diabetes, the underlying mechanisms have yet to be fully determined. In this cross-sectional study, we investigated determinants of aortic stiffness (aortic pulse wave velocity (PWV)) by measuring systemic collagen formation and turnover (plasma concentrations of procollagen type 1 N-propeptide (plasma P1NP)), cardiovascular autonomic function and systemic inflammation (hsCRP), in subjects with type 1 and 2 diabetes, in comparison with impaired glucose tolerance (IGT) subjects.

Fifty males with diabetes (35 type 2, 15 type 1) (age range 39-75yrs) and 21 males with IGT (age range 42-69yrs) were studied. Concentrations of P1NP were higher in type 1 in comparison with type 2 and IGT subjects (40.3±18.3 ug/L versus 28.1±12.5 ug/L versus 30.4±9.8 ug/L respectively, p<0.05) and were positively correlated with aortic PWV in type 1 (r=0.56, p<0.05) and type 2 subjects (r=0.46, p<0.01). Multiple regression analysis revealed age, hsCRP and P1NP to be stronger predictors of aortic PWV in diabetic subjects in comparison with other measured cardiovascular risk factors including autonomic dysfunction.

Our findings highlight the likely importance of increased collagen turnover as a predictor of aortic stiffening in diabetes. P1NP concentration was more strongly predictive of aortic stiffening than conventional risk factors with the exception of age. Further investigation is required to establish whether true differences in collagen turnover exist between type 1 and 2 diabetes.

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P1.57
MODULATION OF ARGINASE IN RESPONSE TO WALL SHEAR STRESS

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Introduction: Aterations of wall shear stress can predispose the endothelium to the development of atherosclerotic plaques. Ample evidence indicates that arginase expression/activity correlates with several risk factors for cardiovascular disease including atherosclerosis. However, the