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4.1: TNF- ANTAGONISTS IMPROVE ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A META-ANALYSIS

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(PWV) and Augmentation Index (Alx) and their determinants from childhood may underlie ethnic variability in CV risk as young adults in the 'DASH' longitudinal study.

Methods: DASH, at <http://dash.sphsu.mrc.ac.uk/>, includes representative samples of 6 main UK ethnic groups [3]. PWV and Alx were recorded using Arteriograph device at ages 21-23y in a sub-sample (n=666) psychosocial, anthropometric and blood pressure (BP) measures were collected then and in 2 previous surveys at the age of 11-13y and 14-16y. For n=334, physical activity (PA) was measured over 5 days (ActivPal).

Results: Unadjusted values and regression models for PWVs were similar or lower in ethnic minority than in White UK young adults [4], while Alx was higher - Caribbean (14.9, 95%CI 12.3-17.0, %), West African (15.3, 12.9-17.7, %), Indian (15.1, 13.0-17.2, %) and Pakistani/Bangladeshi

Methods: Echocardiography and sitting brachial systolic BP (SBP) measurements were performed on 2065 17yr olds. 1377 participants (742 females, 635 males) had complete BP data measured at age 7yrs, 9yrs, 11yrs and 15yrs. LVM was calculated and indexed to height^{2.7} (LVMI). Linear regression was used to investigate associations.

Results: Elevated LVMI at 17yrs was associated with increased SBP at all ages in females and in males at 9yrs, 11yrs, 15yrs and 17yrs (Table 1). Adjustment for cardiometabolic risk factors at age 17 (age, free-fat mass, height, height² and smoking (Model 1)) did not substantially attenuate all LVMI and BP associations and associations at earlier ages remained significant after further adjustment for SBP at age 17.

Table 1

Age (yrs)	Unadjusted		Model 1		Model 1+ SBP at 17yrs	
	Male	Female	Male	Female	Male	Female
7	0.01±0.03	0.09±0.02**	0.02±0.03	0.06±0.02**	-0.02±0.03	0.07±0.02**
9	0.06±0.03*	0.06±0.02*	0.02±0.02	-0.007±0.02	0.02±0.02	-0.006±0.8
11	0.15±0.03**	0.06±0.02**	0.09±0.03**	0.008±0.02	0.09±0.03**	0.009±0.02
15	0.05±0.02*	0.06±0.02**	0.02±0.02	0.04±0.02*	0.02±0.02	0.03±0.02*
17	0.16±0.03**	0.14±0.02**	0.13±0.03**	0.09±0.02**		

Data are $\beta \pm SE(g/m^{2.7})^* = p < 0.05$ ** $p < 0.0001$

(15.7, 13.7-17.7, %), compared with White UK (11.9, 10.2-13.6, %). In multivariate models, adjusted for gender, central sysBP, height and heart rate, Indian and Pakistani/Bangladeshi young adults had higher Alx ($\beta = 3.35, 4.20$ respectively, $p < 0.01$) than White UK with a similar trend for West Africans and Caribbeans but not statistically significant. Unlike PWV, PA, psychosocial or deprivation measures were not associated with Alx, with borderline associations from brachial BP but no other childhood variables.

Conclusion: Early adult Alx, but not arterial stiffness, may be a useful tool for testing components of excess CV risk in some ethnic minority groups.

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3.9

ASSOCIATIONS OF BLOOD PRESSURE THROUGHOUT CHILDHOOD WITH LEFT VENTRICLE MASS IN ADOLESCENCE

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Background: High blood pressure (BP) is a major risk factor for elevated LV mass (LVM) in adults. Evidence suggests that BP tracks from childhood into adolescence and adulthood, however findings on the association between childhood BP and LVM are inconsistent and the temporal relationship between BP in childhood and elevated LVM in adolescence is unknown.

Conclusion: These results show that high antecedent childhood BP from as early as age 7 is associated with higher LVMI in adolescence independent of current BP.

4.1

TNF- ANTAGONISTS IMPROVE ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A META-ANALYSIS

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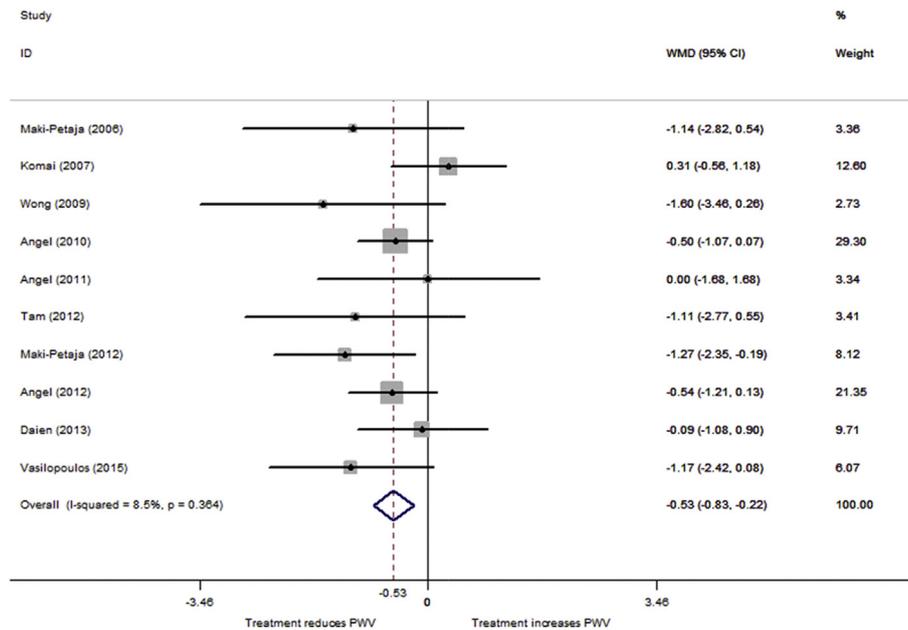
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Purpose/Background/Objectives: Patients with rheumatoid arthritis (RA) have a higher arterial stiffness than their age-matched healthy counterparts and an increased inflammatory burden that might be associated with their increased cardiovascular risk. Tumor necrosis factor alpha (TNF)-antagonists have been found to reduce inflammatory markers in RA however it is debatable if they have favorable effects on surrogate markers of cardiovascular outcomes. We conducted a meta-analysis to assess the effect of TNF-antagonists on arterial stiffness, a predictor of cardiovascular events and mortality, in RA patients.

Methods: A search of PUBMED was conducted to identify studies into the effect of TNF-antagonists on arterial stiffness in RA patients. Data were available on 3 TNF-antagonists: infliximab, adalimumab, and etanercept.

Results: 10 studies (n=208 patients) out of 14 eligible studies in total, measured changes in carotid-femoral PWV after treatment with anti-TNFs. Subjects under therapy with anti-TNFs significantly decreased their arterial stiffness (mean change in PWV: -0.53 m/s, $p = 0.001$)(Figure). No significant heterogeneity was observed across the studies ($I^2 = 8.5\%$, $p = 0.364$). By subgroup analysis, improvement in PWV after therapy was independent of age, sex, nationality and clinical response to treatment and dependent of the type of the TNF- antagonist used.



Conclusions: The balance of evidence suggests that TNF-antagonists may have a beneficial effect on arterial stiffness in RA patients. Given the predictive role of aortic stiffness for adverse cardiovascular outcomes, TNF-antagonists might confer reduction of the cardiovascular risk of these patients beyond their anti-inflammatory effect. However, larger longitudinal studies are warranted to confirm recent findings.

4.2

WITHDRAWAL OF STATINS THERAPY IN PATIENTS AFTER CAROTID ENDARTERECTOMY ASSOCIATED WITH INCREASING RISK OF SIGNIFICANT RESTENOSIS

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Background: The benefit of carotid revascularization is decreased by the occurrence of restenosis at the site of surgery, which is associated with a modestly increased risk of stroke. Preventing restenosis plays pivotal role in the overall treatment and prevention of stroke in patients with carotid artery disease.

Purpose: To evaluate influence of discontinuing of statins therapy on occurrence of restenosis in patients after carotid endarterectomy.

Methods: We studied 240 patients after carotid endarterectomy, mean age – 64.4±6.8 years. All the patients were divided into two groups: 1 group comprised 124 patients, who had taken atorvastatin in dose 10-40 mg daily and 2 group – 116 patients who discontinued statins therapy due complication 3%, poor tolerance 9% or personal reluctance 88%. All the patients also underwent serial standardized ultrasound examination on 1, 3, 6, 12 month during first year after operation and then annually. Mean observation time was 5.6±2.1 years. Significant restenosis carotid artery (more than 70%) was established by standard Doppler velocity criteria.

Results: The significant restenosis of internal carotid artery was found in 2,4% patients with statins therapy and in 7,8% patients without statins. Statins withdrawal increased the incidence of late significant restenosis of internal carotid artery (odd ratio: 3.393 95% confidence interval: 0.895–12.857). Patients with withdrawal of statins had higher wall thickness: 4.3±0.8 against 2.9±0.9 (#1088 $p < 0,05$).

Conclusion: Withdrawal of statins therapy in patients after carotid endarterectomy associated with increasing risk of significant restenosis carotid artery.

4.3

ELECTRONIC CIGARETTE SMOKING INCREASES AORTIC STIFFNESS IN YOUNG SMOKERS

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Purpose/Background/Objectives: Smoking increases aortic stiffness which is an important predictor of cardiovascular risk. Electronic cigarettes (EC) simulate tobacco cigarette (TC) and have been advocated as a less harmful alternative. We investigated the acute effect of EC smoking on aortic stiffness compared to the effect of TC smoking.

Methods: We studied 24 healthy smokers (mean age 30±8 years, 13 females), who were free of risk factors X from smoking. Each participant visited our unit on four separate occasions (96 in total) and smoked: a) TC over 5 minutes b) EC over 5 minutes c) EC for a period of 30 minutes. During the sham procedure, participants did not smoke anything. Carotid-femoral pulse wave velocity (PWV) was used to assess aortic stiffness.

Results: Both TC and EC smoking increased systolic and diastolic BP, and the differences in changes of BP responses between the two smoking forms were not significant. Compared to TC, EC5 min smoking resulted in a less potent PWV increase throughout the study ($F = 4.425$, $P = 0.005$). On the other hand, EC30min resulted in a PWV increase similar to that of TC smoking throughout the study period ($F = 0.268$, $P = 0.615$). EC30 min smoking resulted in a more potent effect on PWV compared to EC5 min smoking ($F = 3.167$, $P = 0.030$).

Conclusions: EC over 30 minutes induces an unfavorable effect on aortic stiffness similar to TC smoking. The influence of EC smoking over 5 minutes on aortic stiffness is not as prompt and is less potent compared to the effect of TC smoking.

4.4

ARTERIAL PHENOTYPE MODULATION AND REGULATION OF VASCULAR FIBROSIS IN MICE BY CONDITIONAL INACTIVATION OF INTEGRIN AV SUBUNIT IN VASCULAR SMOOTH MUSCLE CELLS

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Integrin α_v functions as a receptor for adhesion proteins and is expressed at high density in vascular smooth muscle cells (VSMC)^{1,2,3,4,5} whose phenotypic modulation plays a crucial role in arterial ageing and atherosclerosis^{6,7}.