Objective: Atherosclerosis is an inflammatory disease associated with an imbalance between pro- and anti-inflammatory mechanisms. While ample evidence is available in animal models, less is known about links between local vascular inflammation in human disease. T regulatory cells (Treg) have been implicated in atherosclerosis in mice but links with human vascular inflammation are poorly understood. Accordingly, we aimed to investigate the relationship between Tregs in peripheral blood and locally in perivascular adipose tissue (pVAT) with endothelial function as a key mechanism in pathogenesis of vascular disease.

Design and method: Treg (CD3+/CD4+ /CD25+/FoxP3+) infiltration was studied in pVAT of atherosclerotic coronary artery (CORO), non-atherosclerotic internal mammary artery (IMA), as well as subcutaneous AT and peripheral blood were quantified using flow cytometry from 50 CABC patients (38 M:12 F; age 65±10) with typical atherosclerosis risk factor profile. Vascular function was assessed in IMA segments ex vivo by isometric tension studies of vasorelaxations to acetylcholine and ROS production was measured in vascular segments with 5μM lucigenin enhanced chemiluminescence.

Results: Treg infiltration was observed in both IMA and CORO, but was significantly higher in IMA pVAT than in pVAT surrounding CORO (13.58 ± 15.6 vs. 4.74 ± 6.2 cells/mg; p < 0.01). Moreover, there was a significant correlation between these two AT depots suggesting systemic pVAT regulation (R = −0.53; p = 0.001). Indeed we observed a significant correlation between number of risk factors for atherosclerosis and Treg content (R = 0.33; p = 0.02). Importantly, there was an inverse correlation between Treg content in peripheral blood and ACh-induced vasorelaxations (R = −0.31; p < 0.05). Local T reg infiltration in pVAT was signifi cantly correlated with indices of NO production, as measured by chemiluminescence (R = 0.07; p < 0.007). However, NO production was scavenged by ROS (measured by ratio of L-NAME enhanced/basil superfused levels) and Treg infiltration in pVAT did not correlate with IMA endothelial function (R = −0.02 p = 0.92) or total vascular ROS production (R = −0.12 p = 0.53).

Conclusions: Atherosclerosis is accompanied by local decrease in T regulatory cell content in atherosclerotic vs. non-atherosclerotic arteries, although their amount is linked with classical risk factors for atherosclerosis. Higher peripheral blood T reg levels are associated with better endothelial function, although it is not achieved through locally infiltrating Tregs.

OP.05.06
DIFFERENCES IN ENDOVASCULAR GLYCOXYLAL IN RECENTLY DIAGNOSED AND UNTREATED MIDDLE-AGED HYPERTENSIVE PATIENTS REGARDING INCREASED CARDIOVASCULAR RISK

H. Triantafyllidi, D. Benas, S. Vlachos, A. Schoinas, I. Ikonomidou, G. Pavlidis, L. Palaiodimos, J. Lekakis. Second Department of Cardiology, Medical School, University of Athens, ATTIKON Hospital, Athens, GREECE

Objective: Target organ damage (TOD) evaluation in patients with arterial hypertension is necessary in order to estimate cardiovascular risk (CVR) and plan treatment. Increased carotid intima-media thickness (IMT), an index of TOD, represents the diffuse vascular atheromatosis. The integrity of endothelial glycocalyx (EG) plays a vital role in vascular permeability, inflammation and elasticity and finally to cardiovascular disease. Sideview Darkfield imaging allows for non-invasive automated estimation of EG dimensions based on the erythrocyte column distribution. We aimed to investigate any differences in EG levels in untreated patients with essential hypertension.

Design and method: We studied 86 patients with newly diagnosed and never treated essential hypertension (mean age 53±7 years, 53 males). Increased perfusion boundary region (PBR) of the sublingual arterial microvessels (ranged from 5–25 micrometers) using Sideview Darkfield imaging (Microscan, Glycocheck) was measured as a non-invasive accurate index of reduced EG thickness. We estimated carotid intima-media thickness using carotid ultrasonography (normal levels IMT < 0.8 mm).

Results: The whole population was divided in two groups regarding IMT levels, group A (IMT< 0.8 mm, n = 30, mean age 52±7 years, 17 males) and group B (IMT > 0.8 mm, n = 56, mean age 54±7 years, 36 males). Group A and B were also matched for age and sex. No differences were found within groups regarding 24 h systolic and diastolic ABPM as well as PBR 5–25, PBR 10–19 and PBR 20–25. We found that PBR 5–9 was increased in group B (1.19±0.1 vs. 1.13±0.1, p = 0.04) compared with group A.

Conclusions: EG dimensions are reduced in hypertensive patients with augmented cardiovascular risk. Further studies are needed to confirm our results in a larger population and possibly establish EG measurement as a new cardiovascular risk marker.

OP.2D.07
THE EFFECTS OF ALPHA 1-ADRENOCEPTOR-BLOCKADE BY DOXAZOSIN OR ACE-INHIBITION BY RAMIPRIL ON ENDOTHELIAL FUNCTION IN PRIMARY HYPERTENSION: THE DORA STUDY

A. Jekell, M. Kalani, T. Kahan. Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Division of Cardiovascular Medicine, Stockholm, SWEDEN

Objective: To study whether reducing noradrenergic sympathetic vascular tone by doxazosin or blocking the renin-angiotensin-aldosterone system by ramipril will alter endothelial function in patients with uncomplicated hypertension.

Design and method: Mild-to-moderate hypertensive patients (age 54 ± 12 years, 34% women, blood pressure (BP) 148 ± 11/88 ± 9 mmHg) were randomized double-blind to ramipril (10 mg od, n = 33) or doxazosin (8 mg od, n = 28) for 12 weeks. Endothelium dependent and independent vasodilatation was studied by forearm post-ischemic flow mediated vasodilatation (FMD) and sublingual glyc eryl trinitrate (GTN), respectively, by the forearm skin microcirculation responses to GTN (Ach) and sodium nitroprusside (SNP) applied by iontophoresis, respectively; and by endothelium dependent vasodilatation following beta 2-adrenoceptor-agonist stimulation (sc terbutaline) assessed by the reflection index from pulse wave analysis.

Results: Drug treatment reduced aortic and brachial BP, and reduced indices of aortic stiffness. The effects (mean ± SEM or medians and interquartiles; and mean ± SEM; for delta week 0–12), by ramipril and doxazosin on FMD (5.3 ± 2.4 to 4.5 ± 4.3%, delta -1.1 ± 1.0, and 6.3 ± 4.4 to 5.3 ± 3.1%, delta -0.3 ± 1.0); GTN (14.4 ± 7.0 to 14.4 ± 6.9%, delta 0.3 ± 1.3, and 15.5 ± 6.8 to 14.4 ± 7.0, delta -0.5 ± 1.3); endothelial function index (see FMD/GTN, 0.49 ± 0.56 to 0.44 ± 0.64, delta 0.07 ± 0.12, and 0.47 ± 0.38 to 0.51 ± 0.41, delta 0.07 ± 0.12); and reflection index (–6.8 ± 3.2 to –7.7 ± 3.8, delta –0.8 ± 1.0, and –7.3 ± 2.8 to –6.6 ± 3.1, delta 0.3 ± 0.9) were small. Also the effects by ramipril and doxazosin on skin microcirculation (peak flux, arbitrary units) were small: 33 [18–62] to 28 [19–53], delta -2 ± 5, and 36 [21–62] to 41 [20–67], delta 1 ± 9 by Ach; and 46 [34–84] to 43 [26–87], delta -9 ± 8, and 58 [33–78] to 60 [44–82], delta -0.3 ± 10 by SNP; and 0.5 [0.4–1.0] to 0.8 [0.4–1.3], delta 0.2 ± 0.2, and 0.6 [0.4–1.0] to 0.8 [0.3–1.4], delta 0.3 ± 10 by the peak flux ratio (Ach/SNP), respectively. Also skin microcirculatory responses to heat induced hyperemia remained unchanged.

Conclusions: ACE-inhibition and alpha 1-adrenoceptor-blockade for 12 weeks reduce BP and improve indices of aortic stiffness but appear to have no effects on endothelial function assessed in multiple ways in mild-to-moderately uncomplicated hypertension. Evidence of endothelial dysfunction and the possible benefit of treatment might require more advanced stages of hyper- tension disease.