**Results:** We show that in HT patients,VC was correlated with higher systolic pressure,the higher incidence and more intima-media thickness of the plaque of carotid artery and was associated with arterial stiffness(including higher carotid-femoral pulse wave velocity, aortic systolic pressure, augment pressure, augment index($P < 0.05$)). Furthermore, The phenotype of M1∼like monocyte/ macrophages was significantly increasesd in HT patients with VC ($P < 0.05$)(Fig 3). Although both Serum OPN and OPG levels increased in HT patients with VC, they significantly upregulated anti-inflammatory M2 macrophages marks ($P < 0.05$) and only OPN downregulated pro-inflammatory M1 macrophages marks.

**Conclusions:** The phenotype of M1 macrophages and M2 macrophages is promoted by VC(fig 2). The ability of OPN and OPG to promote differentiation of macrophages into an alternative, anti-inflammatory phenotype may explain their protective effects in VC of HT patients. These data provide novel insight into the link between inflammtion and VC diseases.

## 9A.04 CARDIOVASCULAR RISK FACTOR PROFILE IN AN ITALIAN COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A THREE YEARS FOLLOW-UP

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**Objective:** Rheumatoid arthritis (RA) is a systemic inflammatory disease characterized by an elevated cardiovascular morbidity and mortality, but detailed informations on the risk score profile using different approaches, as well as on the major determinant(s) of the cardiovascular risk of these patients are scanty.

**Design and method:** The present study reports data collected in a cohort of RA patients with CV risk score calculators Framingham and SCORE uncorrected or corrected according to European League against Rheumatism (EULAR) recommendations. Cardiovascular events were recorded during the 3 yrs follow-up, to determine the burden of CV morbidity and the relative impact of traditional CV risk factors and disease activity/severity.
We enrolled in the study 198 pts, 77% females, age $65.0 \pm 11.6$ yrs (means $\pm$ SD), disease duration $13 \pm 9$ yrs. 76% of pts were RF +, 68% ACPA+ and 46% with erosive disease. 3% were smokers and 32% ex smokers. Mean BMI ($24.6 \pm 4.4$), plasma levels of cholesterol (total,HDL,LDL), triglycerides and glucose and prevalence of smokers were comparable with those detected in the local general population, while the prevalence of hypertension and diabetes were significantly higher in both males and females.

**Results:** Risk scores with Framingham were lower than in general population and comparable using SCORE, but the application of 1.5x correction factor for RA, as recommended by EULAR, modified these figures. The number of hypertensive and diabetic pts increased significantly (P<.0001/ .019) during the follow-up as well as the mean values of Framingham and SCORE ($p < .015$/.011). The MI and stroke prevalence were 5% and 2% respectively: the incidence rate/1000 person/year were 8.8 and 3.7 versus 2.7 and 2.6 in the general population. No relation was detectable between disease activity indices and CV events or risk scores.

**Conclusions:** The present study provides evidence that 1) RA is associated with an increased CV morbidity even in the medium follow-up period, 2) risk score needs to be adjusted as by EULAR indications to obtain sensitive assessment of risk and 3) that hypertension represents a major CV risk factor in this population.

## 9A.05 SYMPATHETIC NERVOUS SYSTEM DRIVES RENAL INFLAMMATION BY ALPHA(2A)-ADRENOCEPTORS

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**Objective:** Inflammatory processes play a pivotal role in pathogenesis of chronic kidney disease (CKD). alpha2A-adrenoceptors (alpha2A-AR) in adrenergic neurons are known for regulating sympathetic tone by controlling norepinephrine (NE) release from sympathetic nerve endings by a negative feedback mechanism. Increased sympathetic tone leads to hypertension and the progression of CKD. In addition, there is some evidence that alpha2A-ARs on non-adrenergic cells have modulating effects on the inflammatory response. Here, we tested our hypothesis that deletion of alpha2A-AR exaggerates renal fibrosis.

**Design and method:** Unilateral ureteral obstruction (UUO), a model of renal fibrosis, was performed in FVB mice lacking the alpha2A-AR (KO) and compared to its wild-type (WT). Renal NE tissue content was measured by HPLC. Immunohistochemistry and gene expression analysis were performed 7 days after UUO. Murine macrophages were isolated from the peritoneal cavity, subsequently cultured and stimulated.

**Results:** Renal sympathetic neurotransmission and NE tissue content was significantly exaggerated in KO compared to WT. Despite an increased sympathetic activity, renal fibrosis, assessed by sirius red/ fast green collagen staining ($p = 0.0428$) and renal collagen-1 expression ($p = 0.001$), was significantly attenuated in KO compared to WT 7 days after UUO. Moreover, the expression of the pro-inflammatory and pro-fibrotic cytokines TNF-alpha ($p < 0.05$) and TGF-beta ($p < 0.05$), as well as the chemokines CCL2 ($p < 0.05$) and CCL5 ($p < 0.05$) were significantly reduced in mice lacking the alpha2A-AR compared to WT indicating a pro-inflammatory role of alpha2A-AR on immune cells in the progression of renal fibrosis. In addition, F4/80-staining confirmed the reduced renal infiltration of macrophages in KO. Stimulation of isolated murine peritoneal macrophages from WT mice with the alpha2-AR-agonist UK14.304 (0.1 $\mu$M) induced a 2-fold expression of TNF-alpha ($p < 0.05$).

**Conclusions:** Alpha2A-ARs appear not only to be a key player in regulating sympathetic tone, but also promote inflammation and the progression of renal fibrosis in response to kidney injury. To dissect the cell type and whether adrenergic or non-adrenergic alpha2A-ARs are responsible for these effects further experiments are necessary. Experiments with a transgenic mouse re-expressing the adrenergic alpha2A-ARs are planned. First results give an idea that non-adrenergic alpha2A-ARs could responsible for the observed effects.

## 9A.06 IMPACT OF METABOLIC, HEMODYNAMIC AND INFLAMMATORY FACTORS ON TARGET ORGAN DAMAGE IN HEALTHY SUBJECTS

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**Objective:** We wanted to test the impact of metabolic, hemodynamic and inflammatory factors on target organ damage (TOD) defined as cardiac hypertrophy, atherosclerosis, arterioclerosis and microvascular damage.

**Design and method:** In a population based cohort study of 2115 healthy subjects (1049 male 1066 female) with a mean age of $53.1 \pm 10.5$ without known diabetes or cardiovascular disease we measured fasting plasma glucose (FPG), serum insulin, lipid profile, soluble urokinase receptor (suPAR), c-reactive protein (CRP), urine albumin/creatinine ratio (UACR), 24-hour ambulatory systolic (24hSBP) and diastolic blood pressure (24hDBP), left ventricular mass index (LVMI) by M-mode echocardiography, carotid plaques (CP) by carotid ultra sound and carotid-femoral pulse wave velocity (PWV). To establish best model for association of LVMI, CP, PWV and UACR we used multiple linear regression analysis starting with inclusion of all variables without co-linearity taking away one by one non-significant variables.

**Results:** Cardiac hypertrophy assessed by LVMI was primarily associated with gender ($\beta = 0.37$), 24hSBP ($\beta = 0.26$) and HR ($\beta = -0.15$). Insulin resistance (IR) and inflammation only had minor albeit significant impact on LVMI assessed by HOMA ($\beta = 0.09$) and CRP ($\beta = 0.05$). Atherosclerosis assessed by CP was primarily associated to age ($\beta = 0.31$), 24hSBP ($\beta = 0.13$) and smoking ($\beta = 0.13$). Arteriosclerosis indicated by PWV was primarily associated to age ($\beta = 0.39$), 24hSBP ($\beta$=0.31), gender ($\beta = 0.14$) and HR ($\beta = 0.15$). Additionally, FPG ($\beta = 0.04$), total cholesterol/high density lipoprotein ratio (TC/HDL) ($\beta = 0.04$) and CRP ($\beta = 0.03$) had positive independent impact on PWV. Microvascular damage assessed by UACR was primarily associated to gender ($\beta = -0.16$), 24hSBP ($\beta = 0.09$) suPAR ($\beta = 0.09$), smoking ($\beta = 0.05$) and age ($\beta$=0.05).

**Conclusions:** We conclude that 24hSBP were independently associated to cardiac hypertrophy, arteriosclerosis, atherosclerosis as well as microvascular damage, whereas IR and inflammation were only weakly, independently associated to hypertrophy, arteriosclerosis and microvascular damage in healthy subjects.

## 9A.07 CARDIOVASCULAR TARGET ORGAN DAMAGE IN PREMENOPAUSAL SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AND IN CONTROLS. ARE THERE ANY DIFFERENCES?

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**Objective:** In patients with systemic lupus erythematosus (SLE) a greater prevalence of structural and functional cardiovascular (CV) alterations has been described, possibly explaining the higher incidence of CV events, as compared to subjects matched for age and sex.
Aim of this study was to analyze the presence of target organ damage in premenopausal women with SLE and in controls matched not only for demographic characteristics but also for other cardiovascular risk factors.

**Design and method:** 34 patients with SLE clinically stable (SLEDAI Score 2.5 +/- 1.5) (mean age 32 ± 7 years, range 19–44) and 34 controls matched for sex, age, body mass index (BMI), clinic blood pressure (BP) and antihypertensive treatment (if present), underwent: 24 hours BP monitoring, echocardiography with tissue Doppler analysis (TDI) for the evaluation of left ventricular (LV) structure and of systolic and diastolic function, carotid ultrasound for intima-media thickness (IMT) and carotid distensibility measurement, and pulse wave velocity measurement for aortic stiffness (PWV).

**Results:** By definition no difference was observed for age, sex, BMI and clinic BP values and a similar Framingham risk score was observed between SLE and controls (1.3 ± 2.7 vs 1.5 ± 2.3%, p = ns). No significant differences were observed for all echocardiographic parameters except LV longitudinal systolic function (Sm), an early index of LV systolic dysfunction (see Table). Carotid IMT and distensibility, as well as PWV and the prevalence of an abnormal aortic stiffness were both similar in the two groups. At the logistic analysis, PWV was independently associated with LV mass in controls and with the steroid weekly dose in SLE patients.

| | Controls | SLE | *p* |
|---|---|---|---|
| 24 hours Systolic BP (mmHg) | 117±9 | 115±10 | ns |
| 24 hours Diastolic BP (mmHg) | 74±7 | 73±10 | ns |
| 24 hours Heart Rate (bpm) | 75±9 | 81±9 | 0.005 |
| LV mass index ($g/h^{2.7}$) | 27±6 | 28±6 | ns |
| Relative Wall Thickness | 0.29±0.4 | 0.28±0.5 | ns |
| Sm cm /sec | 9.6±1.4 | 9.0±1.3 | 0.038 |
| PWV (m/s) | 6.98±0.73 | 6.77±0.80 | ns |
| IMT (mm) | 0.44±0.07 | 0.44±0.07 | ns |
| Distensibility ($kPa^{-1}$ $10^{-3}$) | 19.4±6.4 | 22.2±10.0 | ns |

**Conclusions:** In patients with SLE and low activity index of the disease we did not observe significant vascular alterations as compared to controls with similar cardiovascular risk. The early LV systolic impairment observed in this group of patients needs confirmation in larger cohorts.

## 9A.08 INTERLEUKINS 33 AND 1B SERUM LEVELS ARE CONNECTED TO COMMON CAROTID ARTERIES REMODELING IN HYPERTENSIVE PATIENTS WITH OBESITY

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**Objective:** To investigate interrelations between interleukin 33 (IL-33) and 1B (IL-1B) serum levels and common carotid arteries (CCA) remodeling in hypertensive patients with obesity.

**Design and method:** 80 hypertensive patients (51 obese) have been observed. An ultrasound examination of CCA with estimation of its geometrical type was performed (cut-off value for vascular wall hypertrophy was vascular segment mass >0,275 g/cm, concentric remodeling was diagnosed with relative wall thickness of CCA >0,2). IL-33 and IL-1B serum levels were estimated using ELISA.

**Results:** IL-33 and IL-1B levels were higher in hypertensive patients (p < 0,001), independently of BMI. Cluster analysis was made to reveal both cytokines' levels impact on CCA geometry. IL-33>73 pg/ml, IL-1B>25 pg/ml was associated with 80,0% prevalence of normal CCA geometry and 20,0% of its concentric hypertrophy. IL-1B>20 pg/ml with IL-33 < 71 pg/ml was characterized by 80,0% prevalence of normal geometry, 10,0% of non-hypertensive concentric remodeling of CCA, 5,0% of concnetric and 5,0% of eccentric hypertrophy. IL-33>71 pg/ml with IL-1B<25 pg/ml was associated with decrease of normal CCA geometry prevalence to 50,0% with increase of concentric hypertrophy rate to 41,7%; other 8,3% patients had eccentric hypertrophy of CCA. IL-33<71 pg/ml, IL-1B<20 pg/ml (p>0,05 vs control group) had 57,9% of normal geometry, 15,8% of concentric remodeling, 15,8% of concnetric hypertrophy and 10,5% of eccentric hypertrophy of CCA.

**Conclusions:** IL-33 and IL-1B serum levels were elevated in hypertensive patients independently of presence of obesity. A pronounced isolated increase in IL-33 level was associated with abrupt increase of CCA hypertrophy prevalence, especially its concentric variant. Accompanying increase in IL-1B level reduced this effect.

## 9A.09 PROTECTION AGAINST COMPLEMENT ACTIVITY IS REDUCED IN ARTERIAL HYPERTENSION

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**Objective:** Different elements contribute to arterial hypertension (HTN) etiology. Among these, endothelial dysfunction and vascular inflammation are now considered important co-factors. We hypothesized that distinctive molecular pathways of endothelial activation are present in HTN patients.

**Design and method:** 6 HTN patients, free of any other condition that may have affected the vascular endothelium, (mean[SD] age 40[11], 67% female) and 13 healthy controls (age 39[10], 37% female) participated. Endothelial cells (ECs) were harvested from a superficial forearm vein through 20-gauge angiocatheter by inserting 3 endovascular wires sequentially under sterile conditions. ECs were washed from wires and fixed on slides. Each harvesting yielded 2000–5000 ECs. Purified ECs were stained for immunofluorescence.

**Results:** We identified reduced expression of CD59, a plasma membrane-bound protein that prevents the final assembly of the terminal complement complex (TCC), in HTN patients compared to controls (0.2551 vs 0.5790, p = 0.05). In vitro experiments confirmed an increased complement deposition/activity in CD59-knockout endothelial cells vs controls. (C5b-9 positivity[SD] 23.3[4.8]% vs 8.3[2.8]%, p < 0.05)

**Conclusions:** Protein expression is similar among arterial and venous endothelial cells, but venous ECs are not subject to the direct effect of elevated blood pressure, since they are located in low-pressure districts barely influenced by arterial blood pressure. Therefore, an increased arterial blood pressure cannot be the cause of this protein dysregulation. On the contrary, we suggest that the presence of reduced CD59 expression may be a co-factor in the development of arterial hypertension and the increase in vascular risk.