



## Artery Research

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### **3.6: OSTEOPROTEGERIN IS ASSOCIATED INDEPENDENTLY WITH AORTIC STIFFNESS IN PATIENTS WITH ATHEROSCLEROSIS AND IN HEALTHY SUBJECTS**

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plus secondary endpoints occurred in 6 patients (24%) in the celiprolol group and in 17 patient (61%) in the control group (hazard ratio, 0.31; 95% CI, 0.14 to 0.71;  $P = 0.0097$ ).

**Conclusions:** Celiprolol effectively reduced both vascular complications and organ ruptures in vEDS patients.

### 3.4

#### A PRESSURE-INDEPENDENT ARTERIAL REMODELLING AND AORTA DILATION IN TREATED PATIENTS WITH FABRY DISEASE

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**Purpose:** Fabry disease is a deficiency of lysosomal enzyme  $\alpha$ -galactosidase A leading to accumulation of glycosphingolipids in cardiac and vascular tissues. After long-term enzyme replacement treatment, we described a continuous vascular hypertrophy whereas the aortic stiffness was paradoxically decreasing. Preliminary results reported aorta dilatation in treated patients. The objective of this study was to determine the prevalence of aortic dilatation, and the relationship between aorta dilatation, aortic stiffness and arterial remodeling in treated Fabry patients.

**Methods:** Case-control study in 34 Fabry males patients ( $38 \pm 12$  yrs) receiving enzyme infusions every other week ( $3.5 \pm 1.5$  yrs), age-matched with 34 controls. All patients and subjects had arterial measurements of a) carotid IMT and diameter, pulse pressure (PP) and stiffness obtained with echotracking; b) aortic stiffness obtained through carotid-femoral PWV and c) aorta diameters (sinus, ascending and descending tubule, arch aortic) assessed by MRI examinations.

**Results:** Aorta root dilatation ( $>40$  mm at sinus) was observed in 13 FD patients (35%), but not at others segments. In controls, sinus diameter was positively correlated with age, aortic and carotid stiffness in univariate analysis ( $R = 0.59$ ,  $P < 0.005$ ;  $R = 0.53$ ,  $P < 0.005$  and  $R = 0.68$ ,  $P > 0.0001$  respectively) and with both age and CPP in multivariate analysis ( $R = 0.59$ ,  $P < 0.005$ ;  $R = 0.53$ ,  $P < 0.005$ , respectively). No relationship in Fabry patients were found in the same univariate and multivariate analysis. Carotid IMT is positively correlated with PP in controls, but not in Fabry patients.

**Conclusion:** This study highlight the pressure-independent arterial hypertrophy and aorta dilatation in treated Fabry patients.

### 3.5

#### IMPROVEMENT IN AORTIC STIFFNESS AFTER ONE YEAR OF ANTI-TUMOR NECROSIS FACTOR- THERAPY IN PATIENTS WITH INFLAMMATORY ARTHROPATHIES IS ASSOCIATED WITH REDUCTION IN CALPROTECTIN (A PROINFLAMMATORY S100 PROTEIN)

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**Background:** Chronic inflammatory arthropathies such as rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are associated with an increased risk of cardiovascular disease. TNF- $\alpha$  antagonists are previously reported to improve vascular function in these patients and thus be beneficial with regard to cardiovascular disease.

**Aims:** To examine the effect of one year treatment with Tumor Necrosis Factor (TNF)- $\alpha$  antagonists on arterial stiffness and carotid intima media

thickness (cIMT) in patients with inflammatory arthropathies, and furthermore to explore possible associations between changes in the vascular measurements and Calprotectin which is a proinflammatory protein (S100A8/S100A9) associated with both inflammatory arthropathies, endothelial dysfunction and acute coronary events.

**Methods and Results:** A total of 53 patients with RA, AS or PsA and clinical indication for anti-TNF- $\alpha$  therapy were included. 36 patients started with anti-TNF- $\alpha$  therapy and were compared with a non-treatment group of 17 patients. Aortic pulse wave velocity (aPWV), augmentation index (Alx) (Sphygmocor), cIMT (ArtLab) and Calprotectin were measured at baseline and after one year. aPWV (mean  $\pm$  SD) was reduced in the treatment group, but not in the control group ( $-0.51 \pm 0.80$  m/s versus  $0.11 \pm 0.48$  m/s, respectively;  $P = 0.001$ ). Alx and cIMT did not change in any of the groups. In the treatment group, change in aPWV correlated with change in Calprotectin ( $r = 0.36$ ,  $P = 0.04$ ).

**Conclusion:** These findings indicate that long term anti-TNF- $\alpha$  therapy improves aortic stiffness in patients with inflammatory arthropathies, and that the improvement is correlated with reduction in the proinflammatory protein Calprotectin.

### 3.6

#### OSTEOPROTEGERIN IS ASSOCIATED INDEPENDENTLY WITH AORTIC STIFFNESS IN PATIENTS WITH ATHEROSCLEROSIS AND IN HEALTHY SUBJECTS

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**Background:** Arterial stiffening is an independent predictor for cardiovascular mortality. Preliminary studies have shown that arterial calcification may have impact on increased vascular stiffness. However, little is known about the role of calcification inhibitor osteoprotegerin (OPG) as an independent predictor of arterial stiffness in patients with peripheral arterial disease (PAD) and in healthy subjects.

**Aim:** To evaluate the association between OPG level and arterial stiffness parameters in patients with PAD and in healthy subjects.

**Materials and methods:** We studied 59 males with PAD (age  $63 \pm 7$  years) and 44 healthy subjects (age  $54 \pm 7$  years). Serum OPG level was measured using ELISA kit. Arterial stiffness parameters, such as aortic pulse wave velocity aPWV and augmentation index, were determined by applanation tonometry using the Sphygmocor device.

**Results:** OPG level ( $5.40 \pm 1.77$  vs  $4.19 \pm 1.14$  pmol/L;  $p < 0.001$ ) and aPWV ( $9.86 \pm 2.31$  vs  $7.69 \pm 1.66$  m/s;  $p < 0.001$ ) were different for the patients and for the controls. There was linear relationship between OPG level and aPWV in patients with PAD ( $R = 0.51$ ,  $p = 0.0001$ ) as well as in healthy individuals ( $R = 0.47$ ;  $p = 0.002$ ). In multiple regression models, OPG level was independently associated with aPWV along with age and mean arterial pressure in the patient group ( $R^2 = 0.34$ ;  $p = 0.034$ ) as well as in the controls ( $R^2 = 0.49$ ;  $p = 0.037$ ).

**Conclusion:** The independent association between OPG level and aPWV in patients with PAD and in controls suggests that calcification inhibitor OPG may be important in the process of aortic stiffening in atherosclerosis and in healthy subjects.