



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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### **P2.03: EARLY INFLAMMATION CAN PREDICT ARTERIAL STIFFNESS: A 15-YEAR LONGITUDINAL STUDY OF 102 PATIENTS WITH RHEUMATOID ARTHRITIS**

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**To cite this article:** S.A. Provan, K. Angel, A.G. Semb, P. Mowinckel, S. Agewall, D. Atar, T.K. Kvien (2008) P2.03: EARLY INFLAMMATION CAN PREDICT ARTERIAL STIFFNESS: A 15-YEAR LONGITUDINAL STUDY OF 102 PATIENTS WITH RHEUMATOID ARTHRITIS, Artery Research 2:3, 107–107, DOI: <https://doi.org/10.1016/j.artres.2008.08.369>

**To link to this article:** <https://doi.org/10.1016/j.artres.2008.08.369>

Published online: 21 December 2019

activity (SLEDAI 18.74±8.25) and 72 controls (age 37.42±9.15) women. Alx was assessed non-invasively by applanation tonometry (Sphygmocor v.7.01, AtCor Medical).

**Results:** Using one-way ANOVA the overall difference of means of Alx between RA (24.71±11.52), SLE (20.81±12.29) and control groups (13.24±10.44); ( $p<0.001$ ) was obtained. Post hoc tests revealed that Alx significantly differed between control group and each of disease groups ( $p=0.006$  for SLE vs controls;  $p<0.001$  for RA vs controls) however there was no difference between groups of SLE and RA ( $p=0.253$ ). Adjustment for the other confounding factors, such as age, mean blood pressure, body mass index, fasting lipids and creatinine was made with a help of stepwise linear regression. However it did not change results. Variable indicating the presence of any of diseases was significant in the model for Alx ( $p<0.001$ ).

**Conclusions:** RA and SLE are associated with increased arterial stiffness. The presence of both diseases contributes to increased augmentation index values and the damage of arterial wall.

doi:10.1016/j.artres.2008.08.368

## P2.03

### EARLY INFLAMMATION CAN PREDICT ARTERIAL STIFFNESS: A 15-YEAR LONGITUDINAL STUDY OF 102 PATIENTS WITH RHEUMATOID ARTHRITIS

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**Objectives:** To examine impact of early inflammation in RA on the development of CV disease.

**Methods:** 238 patients with RA of less than 4 years duration at inclusion in 1992 have been followed longitudinally. At the 15-year follow-up we performed Pulse wave analysis assessments including measurements of AI and PWV using the Sphygmocor apparatus (Atcor). The measurements were corrected for age, sex, MAP and heart rate. The AI was also corrected for height. Patients aged over 70 at the follow-up were omitted from the PWV analysis. Baseline measures of disease activity were then entered consecutively into the model.

**Results:** 102 patients were eligible for analysis of AI, 76 for PWV. Table 1 presents the adjusted univariate  $\beta$  coefficients (CI)/ $p$  for the prediction of AI and PWV. In the multivariate model anti-CCP remained a significant predictor of AI  $p=0.01$ .  $R^2$  adjusted increased from 0.43 to 0.46. In an alternative model without antiCCP, CRP remained a significant predictor  $p=0.04$ ,  $R^2$  adjusted 0.45. In the multivariate model CRP remained a significant predictor of PWV  $p=0.02$ .  $R^2$  adjusted increased from 0.50 to 0.53.

Table1 Variable	AI (dependent variable)	PWV(dep. variable)
CRP	0.12 (0.00-0.25)/0.04	0.03(0.01-0.6)/0.02
ESR	0.06 (-0.008-0.14)/0.08	0.001 (-0.02-0.02)/0.93
IgMRF	0.02 (0.002-0.03)/0.03	0.002(-0.003-0.003)/0.89
Anti-CCP	0.02(0.004-0.03)/0.01	0.003(-0.003-0.003)/0.84
HAQ (health status)	1.67(-0.89-4.22)/0.20	0.46 (-0.05-0.99)/0.08
Sharp (radiographic)	0.09(-0.06-0.25)/0.23	-0.01 (-0.04-0.02)/0.60

**Conclusion:** Inflammation early in the disease course is associated with an increased augmentation index and pulse wave velocity after 15 years.

doi:10.1016/j.artres.2008.08.369

## P2.04

### ASSOCIATION BETWEEN OSTEOPONTIN AND ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Aim:** Osteopontin (OPN) is a pleiotropic cytokine involved in the regulation of mineralization, expressed in bone and kidney, whose levels are elevated during and inflammation. We evaluated the possible relationship between OPN and arterial stiffness in patients with rheumatoid arthritis (RA).

**Methods:** In 40 RA patients (56±5 years, 32 females) and 40 age and sex-matched healthy volunteers, applanation tonometry (Sphygmocor®) was applied for measuring augmentation index (Alx) and carotid to femoral pulse wave velocity (PWV). Endothelium-dependent (flow-mediated dilation, FMD) and independent (sublingual glycerol trinitrate, GTN, 25 µg) vasodilation

were assessed by ultrasound and computerized analysis of brachial artery diameter changes. Plasma levels of OPN and C-reactive protein were also evaluated

**Results:** OPN levels resulted higher in RA patients than in healthy controls (13.3±9.8 vs 5.4±3.1 ng/ml;  $p<0.05$ ). PWV (8.7±2.5 vs 7.6± m/s;  $p<0.05$ ), Alx (30.8±8.3 vs 26.1±7.9 units;  $p<0.05$ ) and FMD (6.1±3.2 vs 7.2±3.2%;  $p<0.05$ ) were significantly different in RA patients than controls. In RA patients, log-transformed OPN was related to PWV ( $r=0.41$ ;  $p<0.01$ ), but not to Alx, FMD or response to GTN. Log-OPN levels correlated significantly also with age ( $r=0.37$ ;  $P<0.01$ ), and log CRP ( $r=0.31$ ;  $p<0.05$ ). In multiple regression analysis ( $r^2=0.35$ ) including age, mean blood pressure and logCRP, logOPN remained a significant predictor of aortic PWV ( $p<0.05$ ).

**Conclusions:** RA patients are characterized by elevated OPN levels, increased arterial stiffness and endothelial dysfunction. The selective, independent relationship between OPN levels and aortic PWV suggests that OPN might represent an important marker/mechanisms for increased arterial stiffness in RA patients.

doi:10.1016/j.artres.2008.08.370

## P2.05

### CENTRAL PULSE PRESSURE IN END-STAGE RENAL DISEASE: THE ROLE OF AORTIC DIAMETER, AORTIC STIFFNESS AND WAVE REFLECTION

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**Objectives:** To assess the determinants of central pulse pressure (CPP) in end stage renal disease (ESRD), with special focus on respective roles of wave reflection, aortic stiffness and geometry (diameter) compared with controls (CT).

**Methodology:** 115 ESRD (49±15 years, SBP/DBP: 152±3/82±1 mmHg) were compared to 59 CT without renal insufficiency (46±13 years (NS), 143±3 (<0.02)/87±2 mmHg (NS)). Cardiac echography (stroke volume (StVl), aortic diameter), carotid artery wave analysis, aortic wave reflections (tonometry) and aortic pulse wave velocity (PWV) were measured, with calculation of characteristic impedance ( $Z_c$ , dyne.s.cm<sup>-5</sup>). Multiple regression analyses were based on 2 models: M1: age, BP, cardiac function, AI% and  $Z_c$ , and M2: age, BP, cardiac function, AI%, PWV and Aortic diameter (to assess determinants of  $Z_c$ ).

**Results:** Versus CT, ESRD had higher carotid pressures, heart rate, AI%, and PWV while aortic diameter was similar. Determinants of CPP in ESRD were age, MBP, cardiac StVl, AI% and  $Z_c$  (M1 model:  $R^2=0.70$ ,  $p<0.001$ ), in CT: MBP, AI% and  $Z_c$  ( $R^2=0.67$ ,  $p<0.001$ ). M2 model shows in ESRD: age, MBP, AI%, Aortic diameter and PWV ( $R^2=0.61$ ,  $p<0.001$ ). In CT, determinants were AI% and PWV ( $R^2=0.46$ ,  $p<0.001$ ) with no impact of aortic geometry. **Conclusion:** Increased CPP is associated with increased arterial  $Z_c$  and wave reflections. In controls, CPP is linked to stiffness and AI% only, and in ESRD: mainly stiffness and AI% plus minor impact of aortic geometry. In normal subjects and hypertensives without renal failure, CPP is determined by stiffness and reflection, but not by aortic geometry.

doi:10.1016/j.artres.2008.08.371

## P2.06

### LEVELS OF NT-PROBNP ARE ASSOCIATED WITH ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** We wished to investigate the association between arterial stiffness and NT-proBNP, a biomarker released in response to atrial and ventricular stretch (RA).

**Methods:** AI and PWV were measured using the Sphygmocor apparatus (Atcor) in 108 patients, 92 patients had acceptable AI, 95 patients acceptable PWV readings. The patients are included in the Euridiss register, an ongoing longitudinal study of Rheumatoid Arthritis (RA) disease activity. Cardiovascular end-points were assessed at the 2007 follow-up. AI and PWV were corrected for age, sex, MAP and heart rate and were dependent variables in separate models. AI was also corrected for height. Multivariate linear regression analysis with NT-proBNP as a continuous variable and ANOVA analysis with quartiles of NT-proBNP were performed.

**Results:** NT-proBNP was associated to PWV in the multivariate linear regression  $\beta$ (CI) 0.024 (0.002-0.046)  $p=0.03$ .  $R^2$  adjusted 0.57  $R^2$  change 0.02  $p=0.03$ . The ANOVA analysis is shown below. NT-proBNP was not associated to AI  $\beta$ (CI) 0.072 (-0.026-0.170)  $p=0.15$ .