



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### **P10.01: AORTIC STIFFNESS IN POLYMYALGIA RHEUMATICA: EFFECTS OF STEROID TREATMENT**

G. Pucci, R. Hijazi, L. Settimi, E. Bartoloni Bocci, M. Pirro, R. Gerli, E. Mannarino, G. Schillaci

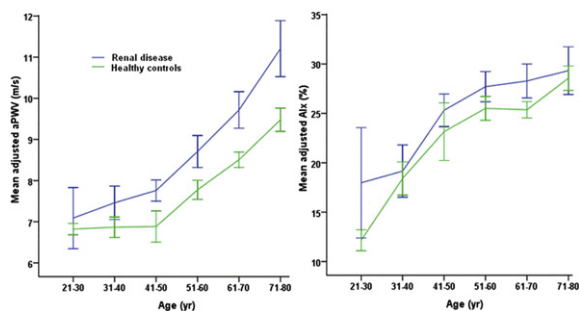
**To cite this article:** G. Pucci, R. Hijazi, L. Settimi, E. Bartoloni Bocci, M. Pirro, R. Gerli, E. Mannarino, G. Schillaci (2010) P10.01: AORTIC STIFFNESS IN POLYMYALGIA RHEUMATICA: EFFECTS OF STEROID TREATMENT, Artery Research 4:4, 175–176, DOI: <https://doi.org/10.1016/j.artres.2010.10.104>

**To link to this article:** <https://doi.org/10.1016/j.artres.2010.10.104>

Published online: 21 December 2019

	Kidney disease	Healthy controls
Age (y)	55±14	56±18
Male (%) <sup>*</sup>	66	48
eGFR <sup>*</sup>	43±21	96±30
Syst./Diast	133/80	134/80
BP	±20/11	±19/11
Adj PWV <sup>*</sup>	9.0±2.5	7.8±1.8
Adj Alx <sup>*</sup>	26.0±9.2	19.3±8.5

**Methods:** Cardiovascular risk factor data, aPWV and Alx were obtained from CKD patients at 8 UK renal centres and participants in ACCT, a study of the general population. Those with diabetes and/or vascular disease were excluded. The relationship of age to aPWV and Alx was compared between patients with CKD (stages 1-5, not on dialysis, non-vascular diagnosis, n=524) and controls (eGFR >60ml/min, n=1535). Controls were stratified by age and gender to ensure comparability.



**Results:** Adjusted aPWV and Alx were higher in CKD patients ( $P<0.001$ ). There was a significant interaction ( $P<0.001$ ) between age and the presence of CKD on aPWV, but this was not seen for Alx ( $P=0.19$ ).

**Conclusions:** Kidney disease in the absence of co-morbidities is associated with increased arterial stiffness compared to controls. In CKD patients aPWV increases more rapidly with age than controls but there was no difference in the pattern of change of Alx with age between groups.

#### P9.10 IN THE ELDERLY, ENDOTHELIAL DYSFUNCTION AND LOW-GRADE INFLAMMATION DO NOT PLAY A PROMINENT ROLE IN LOCAL ARTERIAL STIFFENING – THE HOORN STUDY -

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**Purpose:** To investigate, in the elderly, the association between plasma biomarkers of endothelial dysfunction (ED) and low-grade inflammation (LGI) on the one hand and greater local arterial stiffness of the carotid, femoral and brachial arteries on the other.

**Methods:** Plasma biomarkers for ED (vWf, sVCAM-1, sE-selectin, sICAM-1) and LGI (CRP, SAA, IL6, TNF- $\alpha$ , sICAM-1) were determined and combined into mean z-scores, in a cohort stratified by glucose tolerance status (GTS) (n=745; DM2=275, IGM=183, NGM=287; age 68.7±7.0 years). Ultrasonography was used to measure arterial properties and local arterial stiffness estimates were calculated: distensibility (DC) and compliance coefficients (CC), in all arteries, and the carotid Young's elastic modulus (YEM). Linear regression analyses were used to investigate the above associations.

**Results:** The study population was characterized by a high prevalence of prior cardiovascular disease (CVD) (48%), hypertension (70%) and use of

lipid-lowering (17%) and anti-hypertensive (39%) medication. After adjustment for sex, age, mean arterial pressure and GTS, ED was not associated with carotid, femoral or brachial stiffness (e.g. for the carotid artery ( $\beta$  (95%CI): DC: 0.19(-0.24;0.62), CC: -0.01(-0.03;0.02) and YEM: 0.03 (-0.03;0.08)). LGI was not associated with carotid, femoral or brachial stiffness, except for YEM (0.07(0.02;0.12); other data not shown).

**Discussion:** In an elderly population at high CVD risk, ED and LGI were not associated with local arterial stiffness, except for LGI and YEM. This suggests that ED and LGI, as estimated by these markers, do not play a prominent role in arterial stiffening, as estimated by these local arterial stiffness estimates.

#### P9.11 ARTERIAL STIFFNESS IS ASSOCIATED WITH DECREASED KIDNEY FUNCTION IN A PRIMARY CARE POPULATION: RESULTS FROM THE HIPPOCRATES-STUDY

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**Introduction:** Chronic kidney disease (CKD) is associated with cardiovascular morbidity and mortality. A common observation in both CKD and cardiovascular disease is increased arterial stiffness. Although many studies have focussed on patients with advanced CKD or established cardiovascular disease, relatively few studies have investigated whether increased arterial stiffness is predictive of renal damage in a less selected primary-care population.

**Objective:** In this study, we aimed to investigate whether increased arterial stiffness is associated with impaired renal function in a primary care population without overt CKD.

**Design and Method:** We performed a cross sectional analysis of data from the HIPPOCRATES-study, a study investigating hypertension and cardiovascular complications in a primary care population. Carotid-femoral Pulse-Wave Velocity (cfPWV), blood-pressure measurements and laboratory data were available. The estimated Glomerular Filtration Rate (eGFR) was calculated using the Cockcroft-Gault formula, adjusted for the Body Surface Area.

**Results:** We studied 587 patients (283 males). The mean age of the population was 61.1 ± 10.6 years. The mean GFR was 69.8 ± 15.6 ml/min. In a linear regression model unadjusted for age the mean CF-PWV was inversely associated with GFR. ( $\beta$  -0.16;  $p<0.0001$ ). However, this relationship did not persist after correction for age. Body-mass index was an independent determinant of eGFR in both models.

**Conclusion:** In a primary care population carotid-femoral PWV is significantly associated with decreased kidney function, however this effect is mainly determined by age and body-mass index.

#### Therapeutic Aspects

##### P10.01 AORTIC STIFFNESS IN POLYMYALGIA RHEUMATICA: EFFECTS OF STEROID TREATMENT

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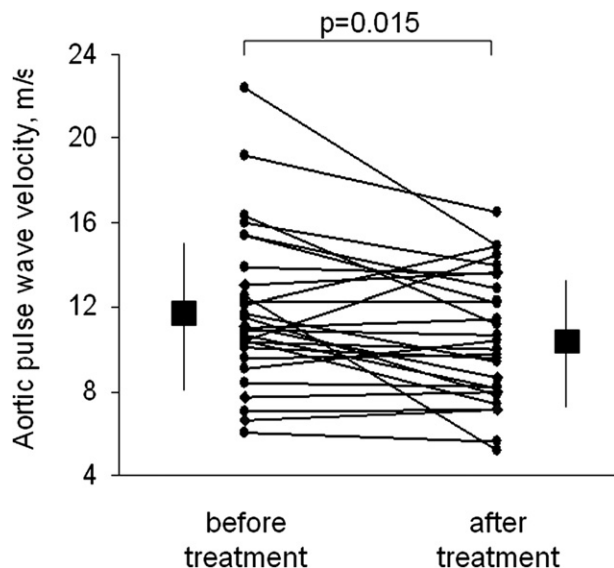
Increased arterial stiffness and cardiovascular risk have been observed in inflammatory diseases. Polymyalgia rheumatica (PMR) is a disease which affects primarily the elderly and exhibits evidence of a systemic inflammatory response, but little is known about aortic involvement in PMR. We investigated whether aortic stiffness is increased in PMR and whether it improves after steroid treatment.

Thirty-nine PMR patients (age 72±8 years, men 45%, blood pressure 134/75±16/9 mmHg) and 39 age-, sex- and blood pressure-matched control subjects underwent aortic pulse wave velocity (PWV) determination (applanation tonometry, Sphygmocor). Aortic augmentation as a measure of the impact of the reflection wave on central hemodynamics was also measured, and corrected for heart rate. Twenty-nine of the PMR patients were reexamined after 4-week treatment with prednisone (starting dose, 12.5-50 mg/day).

Aortic PWV was significantly higher in PMR patients than in control subjects (12.4±4 vs 10.2±2 m/s,  $p<0.01$ ). Treatment was followed by a reduction in heart rate (from 78±12 to 70±10 bpm,  $p<0.001$ ), and no significant change in BP (from 134/75±16/8 to 134/75±15/9 mmHg, both  $p=n.s.$ ). As shown in the Figure, aortic PWV decreased significantly after steroid treatment (from 11.8±4 to 10.5±3 m/s,  $p=0.015$ ), and the difference was independent from blood pressure and heart rate changes. Treatment was also associated with a significant reduction in aortic augmentation. Augmentation index

corrected for a heart rate of 75 bpm decreased from  $0.34 \pm 0.07$  to  $0.29 \pm 0.08$  ( $p < 0.01$ ).

**Conclusions:** Polymyalgia rheumatica is associated with increased aortic stiffness, which may improve upon reduction of systemic inflammation determined by treatment with corticosteroids.



**P10.02**  
EFFECT OF ANTIHYPERTENSIVE TREATMENT ON AORTIC STIFFNESS IN A GENERAL POPULATION

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**Objective:** Aortic stiffness, an independent cardiovascular risk factor, is strongly related to age and mean arterial pressure (MAP). In a general population, we investigated effect of antihypertensive treatment on aortic pulse wave velocity (aPWV) with respect to age and MAP.

**Design and Methods:** In a Czech post-MONICA study, we measured aPWV in 1007 subjects, mean age 54.5 years, 55.0% women, 33.8% on antihypertensive medication. We used linear regression analyses to assess effect of antihypertensive treatment on aPWV. As independent covariates we considered: sex, age (MAP), heart rate, body mass index, smoking, and observer.

**Results:** Subjects using antihypertensive treatment were older, had higher SBP, BMI and aPWV ( $P < 0.0001$ ). In analysis adjusted for MAP, but not in unadjusted analysis, use of antihypertensive medication diminished effect of age on aPWV (regression equations, untreated subjects (TRT-0):  $5.74 + 0.032 \cdot \text{age}$  vs. treated patients (TRT-1)  $9.24 - 0.004 \cdot \text{age}$ ; difference of slope,  $F = 28.9$ ;  $P < 0.0001$ ). In both unadjusted (regression equations  $-1.80 + 0.096 \cdot \text{MAP}$  vs.  $6.38 + 0.026 \cdot \text{MAP}$ ; difference of slopes,  $F = 28.7$ ;  $P < 0.0001$ ) and analysis adjusted for age ( $3.81 + 0.037 \cdot \text{MAP}$  vs.  $9.55 - 0.0056 \cdot \text{MAP}$ ; difference of slopes,  $F = 38.9$ ;  $P < 0.0001$ ), use of antihypertensive treatment was associated with smaller increase of aPWV with MAP.

**Conclusions:** In a general population, we observed that use of antihypertensive medication reduce an increase of aPWV with age. The increase of aPWV with blood pressure was also smaller in treated patients compared to untreated subjects. Antihypertensive drugs prevent aortic stiffening even in subjects whose blood pressure is not well controlled.

**P10.03**  
ACTIONS OF VERAPAMIL IN PRODUCING VASCULAR RELAXATIONS

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We have investigated the vascular relaxant actions of verapamil in comparison with the L-type calcium antagonist nifedipine and the putative selective T-type calcium antagonists NNC 55-0396, mibefradil and

thalidomide. Male Wistar rats (250g) were killed by CO<sub>2</sub> overdose, the aorta and vas deferens were removed for organ bath studies and rings of tail artery were set up in small vessel myographs. In rat aorta, verapamil (100  $\mu\text{M}$ ) significantly reduced the maximum contraction to noradrenaline to a similar degree as nifedipine or mibefradil, but thalidomide had no effect. In rat tail artery, verapamil (1-10  $\mu\text{M}$ ) inhibited contractions to calcium restoration both in the presence of phenylephrine and KCl, but the T-type calcium channel blocker NNC 55-0396 (100  $\mu\text{M}$ ) inhibited contractions to calcium restoration only in the presence of phenylephrine, and the L-type blocker nifedipine (10  $\mu\text{M}$ ) inhibited contractions to calcium restoration only in the presence of KCl. Verapamil inhibited nerve-evoked contractions of epididymal, but not prostatic, portions of rat vas deferens, an action shared with the T-type calcium channel blocker NNC 55-0396 and by thalidomide. In contrast, nifedipine inhibited contractions of prostatic portions of rat vas deferens. It is concluded that verapamil produces vascular relaxations by a mechanism that involves aspects of both L-type and T-type calcium channel block.

**P10.04**  
VACCINATION AGAINST INFLUENZA A/H1N1 VIRUS ADVERSELY AFFECTS ENDOTHELIAL FUNCTION, BUT NOT ARTERIAL STIFFNESS, IN HIV INFECTED PATIENTS

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**Purpose:** Vaccines have been shown to induce a transient impairment of endothelial function and arterial elastic properties. Newly developed vaccines against the pandemic influenza A/H1N1 virus have been reported to have a safe cardiovascular profile; however, their impact on endothelial function and arterial stiffness has not been established.

**Methods:** We recruited 25 HIV infected patients (all male, 3 naïve to antiretroviral therapy, mean age  $35 \pm 10$  years) with a good functional status (mean CD4 count:  $719 \pm 273$ ). All were free from overt cardiovascular disease; 14 patients were vaccinated with a single dose of a monovalent, adjuvanted vaccine against influenza A/H1N1.11 patients were subjected to a sham procedure (controls). Measurements were taken prior to, 8 and 48 hours post vaccination. FMD of the brachial artery was used as an index of endothelial function; carotid-femoral PWV as a measure of arterial stiffness. ADMA, IL-6 and sICAM-1 were measured in blood samples. Comparisons were performed by repeated measures ANOVA.

**Results:** Vaccination led to a significant impairment of endothelial function, denoting a diminished bioavailability of nitric oxide that persisted even after 48h (baseline:  $6.5 \pm 4.8\%$ , 8h:  $2.3 \pm 4.9\%$ , 48h:  $1.8 \pm 4.8\%$ ;  $p = 0.05$ ). However, arterial stiffness, as assessed by cfPWV, was not significantly altered (baseline:  $7.2 \pm 1.2$  m/sec, 8h:  $7.0 \pm 1.2$  m/sec, 48h:  $6.8 \pm 0.9$  m/sec;  $p = \text{ns}$ ). ADMA, IL-6 and sICAM-1 levels did not change.

**Conclusion:** Vaccination against influenza A/H1N1 with a monovalent, adjuvanted vaccine leads to endothelial dysfunction in HIV patients, which lasts for at least 48 hours. Given the increased cardiovascular risk of these patients, these findings warrant further research.

**P10.05**  
CALCIUM CHANNEL BLOCKERS USE IS ASSOCIATED WITH A BETTER COGNITIVE PERFORMANCE IN OLDER HYPERTENSIVE PATIENTS WITH SUBJECTIVE MEMORY COMPLAINTS

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**Background:** Hypertension is strongly associated with cognitive decline and a promising target for dementia prevention. Our aim was to investigate the association between different antihypertensive treatments and cognitive performance in elderly hypertensive patients presenting with subjective memory complaints (SMC).