



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### **P1.11: TRUE ANTIHYPERTENSIVE EFFICACY OF SEQUENTIAL NEPHRON BLOCKADE IN PATIENTS WITH RESISTANT HYPERTENSION AND CONFIRMED MEDICATION ADHERENCE**

H.B. Beaussier, F.M. Michael, F.C. Coudore, M.B. Briet, S.P. Peyrard, M.A. Azizi, P.F.P. Plouin, S.L. Laurent, P.B. Boutouyrie, G.B. Bobrie

**To cite this article:** H.B. Beaussier, F.M. Michael, F.C. Coudore, M.B. Briet, S.P. Peyrard, M.A. Azizi, P.F.P. Plouin, S.L. Laurent, P.B. Boutouyrie, G.B. Bobrie (2013) P1.11: TRUE ANTIHYPERTENSIVE EFFICACY OF SEQUENTIAL NEPHRON BLOCKADE IN PATIENTS WITH RESISTANT HYPERTENSION AND CONFIRMED MEDICATION ADHERENCE, Artery Research 7:3\_4, 113–114, DOI: <https://doi.org/10.1016/j.artres.2013.10.042>

**To link to this article:** <https://doi.org/10.1016/j.artres.2013.10.042>

Published online: 14 December 2019

creatinine may indicate subclinical organ damage with a greater risk of cardiovascular disease.

#### P1.08

##### DETERMINANTS OF VASCULAR DAMAGE IN SYSTEMIC LUPUS ERITHEMATOSUS

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**Background:** Systemic Lupus Erythematosus (SLE) is associated with increased cardiovascular risk and early vascular aging. The aim of the study was to evaluate aortic and carotid stiffness, central blood pressure (BP) and wave reflection in women with SLE, in order to identify whether different vascular districts are similarly influenced by disease duration, activity and organ damage.

**Methods:** Medical and pharmacological history were collected. Disease activity and organ damage were evaluated by ECLAM e SLICC/ACR-DI scores, respectively. Pulse Wave Velocity (PWV) and Augmentation Index (AI) were acquired by applanation tonometry, whereas carotid intima-media thickness (IMT) and stiffness were obtained by an automated image analysis system.

**Results:** 46 SLE women were enrolled (age 41±10years, BP 116±16/76±9 mmHg). Mean disease duration was 17±9years, ECLAM 0,9±1, SLICC 0,9±1,5. PWV(7,4±1,5 m/s) was related to age (r=0.52, p<0,001), mean BP (r=0.59, p<0.001), SLICC (r=0.44, p=0,01). AI (22,5±10,6%) was related to age (r=0.58,p<0,001), mean BP (r=0.50,p<0.001), SLICC (r=0.60,p<0,001), cumulative corticosteroid dose (CCD,r=0.40,p=0.03). Carotid IMT was related only to age (r=0.45, p=0.006). Carotid stiffness was related to age(r=0.68,p<0.001), AI (r=0.54,p<0.001), disease duration (r=0.45,p<0.03), CCD (0.52, 0.01). In multiple regression models adjusted for confounders, SLICC remained an independent predictor of PWV (p=0.04,r<sup>2</sup>=0.13) and AI (p=0.04, r<sup>2</sup>=0.16). Conversely, CCD (p<0.001,r<sup>2</sup>=0.25) and SLICC (p=0.02,r<sup>2</sup>=0.01) were independent predictors of carotid stiffness.

**Conclusions:** In a cross-sectional analysis of a cohort of SLE patients, increased arterial stiffness and wave reflection are independently associated with disease-specific organ damage, but not with disease activity or duration; carotid stiffness is also selectively compromised by chronic corticosteroid use.

#### P1.09

##### MILD COGNITIVE IMPAIRMENT IS ASSOCIATED WITH SYSTEMIC VASCULAR DYSFUNCTION

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**Aim:** To evaluate vascular function and structure in subjects with mild cognitive impairment (MCI).

**Methods:** 58 MCI and 22 controls (age 74±5vs75±4years, men 45vs59% p=ns) were recruited. Endothelial function in the brachial artery (BA) was studied by flow-mediated dilation (FMD) and response to glyceryl trinitrate, (GTN), while large artery stiffness was measured as carotid-femoral pulse wave velocity (PWV).

**Results:** MCI and controls had a similar prevalence of established CV disease (14vs13%,p=ns) and traditional CV risk factors (hypertension 50vs54%, diabetes 13vs5%, dyslipidemia 28vs48%, smoking 4vs9%, p=ns for all). MCI showed higher blood pressure (BP) values than controls (pulse pressure 70±16vs62±12mmHg, mean BP 97±9vs91±8 mmHg, p<0.05 for both). PWV tended to be higher in controls compared to MCI (11.0±2.2vs9.9±2.4 m/s, p=0.07) but the difference was not significant after considering mean BP as covariate. MCI and controls showed similar BA diameter baseline shear rate (SR) and response to GTN. In MCI hyperemic SR and SR area under the curve were significantly lower (1591±831vs1175±673s<sup>-1</sup>, 29.7±15,8\*10<sup>3</sup>vs 21.1±14.9\*10<sup>3</sup>, p<0.05 for all) and time to peak was delayed compared to controls (50±16 s59±16s, p<0.05). Mean FMD values, allometrically corrected for baseline BA diameter, were significantly reduced in MCI (4.5±2.9vs2.7±2.9%, p<0.01). The difference remained significant after considering age, mean BP, and SR area under the curve as covariates (p<0.01).

**Conclusions:** Patients with MCI showed a significant reduction in conduit artery endothelial function as well as in microcirculatory function. These data

support the hypothesis that impaired systemic vascular function might hamper cognitive function.

#### P1.10

##### BENEFICIAL EFFECT OF SEQUENTIAL NEPHRON BLOCKADE OF CENTRAL PRESSURE AND LARGE ARTERY REMODELLING IN RESISTANT HYPERTENSION

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**Objective:** We have previously shown that combined renin-angiotensin system blockade (RB) was less effective than sequential-nephron blockade (SNB) for controlling BP in resistant hypertension (RH). Whether this is accompanied with an improvement in the mechanical properties of large arteries is unknown.

**Design and method:** Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) >135 and/or 85 mmHg, despite 4 week with irbesartan (Irb)+HCTZ+amlodipine, were randomised to SNB (n=82) or RB (n=82) for 12 weeks. Central pulse pressure (CPP) and carotid-femoral pulse wave velocity (PWV) were measured by applanation tonometry. High-resolution echotracking system (Walltrack<sup>®</sup>) was used to measure carotid artery diameter (Dcca), wall thickness (WT), circumferential wall stress (CWS), and stiffness. All parameters were measured at baseline and week 12.

**Results:** Baseline clinical characteristics did not differ between groups. dASBP decreased more in SNB (-19±12 mmHg) vs RB (-8±13 mmHg, p<10-6), either for CPP [SNB (-12.8±16.9 mmHg) vs RB (-1.0±9.3 mmHg, p<0.006)] after adjustment on baseline CPP and delta MeanBP. CCA stiffness and PWV decreased similarly in both groups. Dcca decreased more in SNB (-267±46 µm) vs RB (-7.8±39 µm, p=0.01) after adjustment on baseline D and delta ASBP. WT did not differ and CWS decreased more in SNB (-15.2±16.5 kPa) vs RB (-5.2±12.6 kPa, P=0.001).

**Conclusions:** In RH pts, a ttt strategy based on SNB improved CPP to a greater extent than a RB strategy. This may lead to a better target organ damage prevention and CV outcome. SNB improved CWS. Whether this effect is due aldosterone blockade or sodium depletion remains to be investigated.

#### P1.11

##### TRUE ANTIHYPERTENSIVE EFFICACY OF SEQUENTIAL NEPHRON BLOCKADE IN PATIENTS WITH RESISTANT HYPERTENSION AND CONFIRMED MEDICATION ADHERENCE

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**Objective:** We previously showed that sequential-nephron blockade (SNB) was more effective than combined renin angiotensin system blockade (RB) for controlling BP in patients with resistant hypertension (RH). We assessed medication adherence (MA) on the antihypertensive (AHT) response to SNB/RB with a new combined scoring system.

**Design and method:** Pts with daytime ambulatory SBP/DBP (dASBP/dADBP) ≥135 and/or 85 mmHg, despite 4 week with irbesartan (Irb)+HCTZ+amlodipine, were randomised to SNB (n=82) or RB (n=82) for 12 weeks. MA was scored as: (i) plasma Irb concentration; (ii) urinary AcSDKP/creatinine ratio (UR); (iii) last medication intake before visit (LMI); and (iv) pill counting (PC, %). 1 point of MA score was attributed to Irb >20ng/ml, UR >4nmol/mmol, LMI <24h, PC >80%. MA was defined as low (LMA, score ≤2), intermediate (IMA, score =3), and optimal (OMA, score =4).

**Results:** Among 164 pts: 82 had OMA (46 SNB/36 RB), 52 IMA (23 SNB/29 RB) and 30 LMA (13 SNB/17 RB) (NS). LMA pts were younger than SAs pts (50±11 vs. 56±10 yrs, p<0.011). In OMA pts, the difference in dASBP/dADBP between SNB vs RB was significant (-11 [-17 ; -6]/-6 [-9 ; -2] mmHg, p<0.0001/p=0.0025), favoring SNB, whereas in LMA pts the difference between the two groups did not reach significance (-6 [-19 ; 7]/-1 [-10 ; 7] mmHg, p=0.352/p=0.7096).

**Conclusion:** MA has a major effect on BP lowering, differences between SNB and RB being observed in pts with OMA, not in patients with LMA. Combined methods for assessing MA allow determining the true efficacy of AHT strategies in RH pts.

#### P1.12

##### PREDICTIVE COMBINED ROLE OF CALCIUM SCORE AND CAROTIDIMT IN CORONARY ARTERY DISEASE

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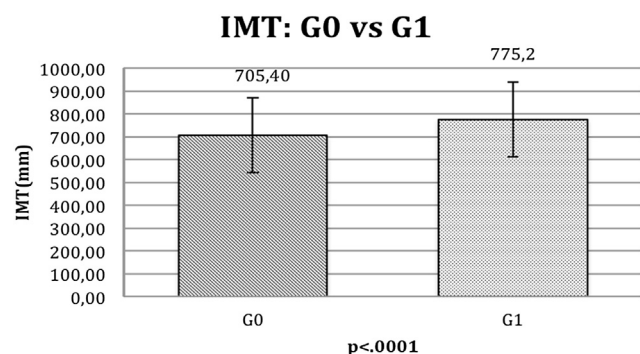
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**Objectives:** up to date the assessment of coronary artery disease (CAD) risk is based mainly on the presence of CV risk factors. However, many markers of subclinical atherosclerosis has been demonstrated as powerful predictors of CV events. Aim of our study was to evaluate if non invasive US parameters, such as carotid properties and heart calcifications, are able to add information to the prediction of CAD.

**Methods:** In 405 in-patients with a clinical indication (overt angina and/or positive exercise test) for coronary angiography (CA), we measured blood pressures (BP), carotid intima-media thickness (IMT), local PWV and distensibility and quantified cardiac calcification by means of Calcium Score (CaS). After CA we divided the group in G1 (N=240) (patients with at least one coronary stenosis >50%), and G0 (N=165) (unaffected coronaries).

**Results:** G0 and G1 patients differed in age ( $67\pm 10$  vs  $64\pm 11$  yrs,  $p=0,01$ ), but not in BMI ( $26\pm 3,5$  vs  $28\pm 16$  kg/m<sup>2</sup>,  $p=0,03$ ); G1 had higher BP ( $130\pm 21/74\pm 10$  vs  $136\pm 18/77\pm 11$  mmHg,  $p<0,02$ ), carotid-IMT ( $705,4\pm 155$  vs  $775,2\pm 164$  mcm,  $p<0,0001$ ), local PWV ( $8,9\pm 2,8$  vs  $9,5\pm 2,7$  m/s,  $p<0,01$ ) and CaS ( $1,51\pm 1,45$  vs  $2,56\pm 1,86$ ,  $p?$ ). Among the considered US parameters, IMT and CaS were the best predictors of CAD, after adjusting for Framingham Risk Score (CaS: OD = 1,  $p<,001$ ; IMT: OD = 1,  $p=0,06$ ).

**Conclusions:** Integrated US of heart and carotid artery can be very useful to detect subclinical ATS in medium-high risk patients, predicting significant CAD and adding qualitative information for better stratify the CV risk and improve clinical management.



#### P1.13

##### THE ASSESSMENT OF VASCULAR AGE IS A USEFUL TOOL TO DEMONSTRATE SUBCLINICAL ARTERIAL DISEASE IN TREATED HYPERTENSIVE PATIENTS

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**Background:** Vascular age may be a more reasonable conception to the patient than the information about the percentage of risk.

**Objective:** To compare degrees of correlation between biological and vascular age with subclinical evidence of arterial disease in treated hypertensive patients.

**Methods:** Subjects in anti-hypertensive treatment, aged 30 to 75 years, were evaluated. Carotid intima-media thickness (cIMT), carotid-femoral pulse wave velocity (cf-PWV), and central parameters were assessed. Vascular age was calculated by the Framingham risk score for general cardiovascular disease. All the patients (n=165) were initially divided in tertiles (T1,T2,T3) according to biological age, and then in relation to vascular age.

**Results:** When divided by biological age, the difference between T3 and T1 was not significant for cIMT ( $0,91\pm 0,14$  vs  $0,88\pm 0,38$  mm) and aortic systolic blood pressure (aSBP;  $136\pm 20$  vs  $129\pm 17$  mmHg) although cf-PWV ( $11,1\pm 2,0$  vs  $9,7\pm 1,5$  m/s,  $p<0,001$ ) and augmentation pressure (AP;  $19\pm 9$  vs  $13\pm 5$  mmHg,  $p<0,01$ ) were significantly higher in T3. When separated by vascular age, the difference between T3 and T1 was significant for all the vascular parameters such as cf-PWV ( $11,9\pm 2,0$  vs  $9,6\pm 1,2$  m/s), cIMT ( $1,10\pm 0,38$  vs  $0,76\pm 0,13$  mm,  $p<0,01$ ), aSBP ( $150\pm 18$  vs  $123\pm 15$  mmHg,  $p<0,001$ ) and AP ( $21\pm 9$  vs  $13\pm 6$  mmHg,  $p<0,001$ ). The correlation was stronger to vascular age than to biological age for AP ( $r=0,46$  vs  $r=0,29$ ), aSBP ( $r=0,57$  vs  $r=0,14$ ) and cIMT ( $r=0,59$  vs  $r=0,39$ ) although similar for cf-PWV ( $r=0,44$  vs  $r=0,40$ ).

**Conclusion:** The assessment of vascular age may be a useful tool to demonstrate the individual cardiovascular risk in treated hypertensive patients.

#### P1.14

##### PULSE WAVE VELOCITY AND KIDNEY DISEASE

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Increased arterial stiffness is one of the major alterations in arterial wall. It can be evaluated in non-invasively way by measuring the pulse wave velocity PWV in large arteries. Increased PWV is an independent predictor factor of cardiovascular complications in patients with hypertension and chronic kidney disease.

We conduct a 2 years prospective study between January 2003 and December 2004. In 161 patients we measured the PWV using an automatic device, the Complior (Colson, Paris). Patients were divided in 4 groups: 43 with polycystic kidney disease (PKD), 38 with primary chronic glomerulonephritis (PCGN), 40 patients with diabetes mellitus (DM) and 40 controls. The 4 groups were matched for age, sex and serum creatinine.

**Results:** we found a positive relationship between age and PWV in the different groups. There was a negative correlation between PWV and creatinine clearance. Among patients with chronic renal failure, PWV were correlated to serum phosphate level ( $p<0,02$ ) and the product calcium X phosphate ( $p<0,006$ ). In patients with DM, PWV was positively correlated to the level of hypertension and to the chronic renal failure (CRF). In patients with PCGN, PWV was positively correlated to the presence of vascular lesions on the kidney biopsy ( $p<0,004$ ), to the level of hypertension and to the CRF. In the PKD group, PWV was correlated to the level of hypertension and to the CRF.

**Conclusion:** PWV is rather related to age, blood pressure and renal function than to type of nephropathy

#### P1.15

##### HIGHER DAY TIME RATE OF SYSTOLIC BLOOD PRESSURE VARIATION IS ASSOCIATED WITH REDUCED RETINAL ARTERIOLAR DIAMETER IN NON-DIABETIC, BUT NOT IN DIABETIC, INDIVIDUALS

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**Background:** Although Type 2 diabetes (T2DM) is associated with retinal vascular disease, the underlying pathophysiological mechanisms are unclear. Reduced retinal arteriolar diameter has been linked to high clinic blood pressure (BP) but the role of more sensitive measures of BP control have never been assessed. This study aimed to determine the relationship between retinal arteriolar diameter and 24 hour ambulatory BP (including BP variability) in people with and without T2DM.

**Methods:** Digitized retinal photographs were analysed to quantify retinal arteriolar diameters in 37 non-diabetic (aged  $53\pm 10$  years; 48.2% male)