



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

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

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### **P29: MECHANISMS OF VASCULAR ENDOTHELIAL GROWTH FACTOR INHIBITION INDUCED HYPERTENSION**

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**To cite this article:** Kaisa Maki-Petaja, Adam McGeoch, Lucy Yang, Annette Hubsch, Carmel McEniery, Fraz Mir, Parag Gajendragadkar, Nicola Ramenatte, Gayathri Anandappa, Christoph Brune, Yoeri Boink, Carola Bibiane-Schonlieb, Paul Meyer, Simon Bond, Ian Wilkinson, Duncan Jodrell, Joseph Cheriyan (2018) P29: MECHANISMS OF VASCULAR ENDOTHELIAL GROWTH FACTOR INHIBITION INDUCED HYPERTENSION, Artery Research 24:C, 87–88, DOI: <https://doi.org/10.1016/j.artres.2018.10.082>

**To link to this article:** <https://doi.org/10.1016/j.artres.2018.10.082>

Published online: 7 December 2019

removal) to aortic mean and diastolic BP. For MoG, central pressure was derived through standard systolic-diastolic calibration (MoGC1) as well as mean-diastolic calibration (MoGC2).

**Results:** Mean±SD differences between device and intra-arterial BP are presented in the Table. There was moderate correlation between device and intra-arterial brachial systolic BP ( $R = 0.58$  XCEL,  $R = 0.47$  MoG,  $P < 0.01$ ) and central systolic BP ( $R = 0.69$  XCEL,  $R = 0.64$  MoGC1,  $R = 0.43$  MoGC2,  $P < 0.01$ ). Intra-arterial central-to-brachial pulse amplification factor was  $1.17 \pm 0.16$  (range 0.88 to 1.55), but there was no correlation between device and intra-arterial amplification ( $R = 0.07$  XCEL,  $R = 0.07$  MoGC1,  $R = 0.19$  MoGC2,  $P > 0.18$ ). Results in sub-groups  $\geq 13$  and  $< 13$  years were similar.

**Conclusion:** Both oscillometric devices overestimated brachial and central systolic/pulse BP, exceeding the validation criteria of  $5 \pm 8$  mmHg, and there was no correlation between intra-arterial and device-derived central-to-brachial pulse amplification. Diastolic BP was acceptable.

Table: Mean±SD of the difference (mmHg) between device and intra-arterial measurements.

	Systolic	Diastolic	Pulse
Brachial XCEL	11.2 ± 8.9	-1.7 ± 6.0	13.0 ± 10.1
Brachial MoG	12.9 ± 11.7	-4.7 ± 5.4	17.9 ± 11.4
Central XCEL	8.8 ± 6.6	-0.7 ± 6.2	9.0 ± 7.7
Central MoGC1	7.7 ± 10.3	-3.1 ± 6.1	10.6 ± 11.6
Central MoGC2	22.3 ± 14.3	-3.2 ± 6.6	25.4 ± 15.0

## P25

### 24-HOUR AORTIC AMBULATORY BLOOD PRESSURE IS BETTER ASSOCIATED WITH COMMON CAROTID ARTERY HYPERTROPHY THAN 24-HOUR BRACHIAL PRESSURE – THE SAFAR STUDY

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**Objective:** Evidence suggests the superiority of office aortic pressure over brachial on the evaluation of vascular damage and prognosis of cardiovascular disease (CVD); 24-hour ambulatory blood pressure monitoring (ABPM) is regarded the optimal method for assessing blood pressure (BP) profile. The non-invasive 24-hour aortic ABPM is feasible and superior to 24-hour brachial regarding the association with left ventricular hypertrophy and diastolic dysfunction. The aim of our study was to examine the association of 24-hour aortic and brachial ABPM with common carotid artery (CCA) hypertrophy.

**Methods:** Consecutive subjects referred for CVD risk assessment underwent 24-hour aortic and brachial ABPM using a validated oscillometric brachial cuff-based device (Mobil-O-Graph). CCA hypertrophy was assessed by high-resolution ultrasound (assessment of intima media thickness - IMT).

**Results:** 497 subjects (aged  $54 \pm 13$  years, 57% men, 80% hypertensives) were examined. Using Hotelling's-Williams test it was shown that 24-hour aortic BP was significantly better correlated with IMT as compared with brachial BP ( $r: 0.254$  vs.  $r: 0.202$  for right IMT,  $r: 0.244$  vs.  $r: 0.207$  for left IMT,  $p < 0.05$ ). Multivariate analysis (adjusted for possible confounders) revealed superiority of 24-hour aortic BP regarding the association with IMT as well as carotid hypertrophy. Last, in ROC analysis, aortic BP had a higher discriminatory ability compared to brachial for the detection of carotid hypertrophy (AUC: 0.707 vs. 0.656 for right carotid artery hypertrophy, AUC: 0.636 vs. 0.602 for left carotid artery hypertrophy,  $p < 0.05$ ).

**Conclusions:** Non-invasively assessed 24-hour aortic pressure is more strongly associated with CCA IMT and provides a higher discriminatory ability for the detection of CCA hypertrophy.

## P27

### INVASIVE CENTRAL PULSE PRESSURE IS RELATED TO AORTIC ROOT DILATATION

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**Background:** Aortic root dilation is an established risk factor for aortic dissection. Despite the relations between aortic root remodeling, carotid-femoral pulse wave velocity (cfPWV) and aortic blood pressure have been advocated by several clinical studies and is supported by physical law, invasive data are lacking. We aimed to investigate the relationship between aortic root remodeling, invasively-measured central blood pressure and cfPWV in patients referred for invasive hemodynamic evaluation for suspected coronary disease.

**Methods:** In 71 patients aortic pulse pressure (aoPP) was measured in the proximal aorta with a calibrated fluid-filled pressure catheter. Before entering the hemodynamic room all patients underwent 2D echocardiographic quantification of aortic root diameter and measurement of cfPWV. Aortic root diameter was then expressed into z-score following age, sex and height adjusted reference values (1).

**Results:** Mean age was  $67 \pm 10$  years and 76.1% of patients were men. Invasive aortic systolic pressure was  $146 \pm 23$  mmHg, diastolic pressure was  $78 \pm 13$  mmHg, and aoPP was  $68 \pm 21$  mmHg. Aortic Z-score was  $-0.32 \pm 1.7$ , while CfPWV was  $9.8 \pm 3$  m/s. While  $\text{Log}_{10}\text{cfPWV}$  and aoPP showed a positive relation ( $r=0.426$ ,  $p<0.01$ ) while aoPP and aortic Z-score were inversely associated ( $r = -0.271$ ,  $p = 0.02$ ). In a multivariable linear regression analysis, Z-score and  $\text{Log}_{10}\text{cfPWV}$  were statistically-significant independent predictors of aoPP ( $p = 0.01$  and  $p < 0.01$ , respectively) after adjustment for age, sex, BSA, heart rate, invasive MBP, and stroke volume.

**Conclusions:** In a population referred to invasive coronary hemodynamic evaluation for suspected coronary disease, aortic root remodeling and aortic stiffness were independently associated with a lower aoPP.

## References

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## P29

### MECHANISMS OF VASCULAR ENDOTHELIAL GROWTH FACTOR INHIBITION INDUCED HYPERTENSION

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**Introduction:** Drugs targeting Vascular Endothelial Growth Factor (VEGF) signaling pathway are approved therapies for cancer. Unfortunately, VEGF

inhibitors lead to hypertension in 30-80% patients. Reduced nitric oxide synthase activity and increased vascular resistance have been proposed as potential mechanisms. We aimed to assess these mechanisms in oncology patients receiving VEGF inhibitor, pazopanib (NCT01392352).

**Methods:** 27 normotensive patients received pazopanib 800mg od. Endothelial function was assessed using forearm plethysmography with intra-arterial infusion of Acetylcholine (ACh), Sodium Nitroprusside (SNP) and L-N-monomethyl-arginine (L-NMMA). Also, Blood Pressure (BP), Pulse Wave Velocity (PWV), Cardiac Output (CO), and Peripheral Vascular Resistance (PVR) and capillary density in the eye were assessed. All measurements were taken at baseline, 2 and 12 weeks after initiation of the treatment.

**Results:** Following 12 weeks of treatment, systolic BP rose by 12 (95% CI:4–19) mmHg;  $P = 0.003$ , diastolic by 10 (95% CI:5–15) mmHg;  $P < 0.001$ , PWV by 1.3 (95% CI:0.3–2.2) m/s;  $P = 0.01$ , PVR by 11.1 (95% CI:7.7–14.6) mmHg $\cdot$ L/min;  $P < 0.001$ . Capillary density in the sclera reduced by  $12 \pm 18\%$ ;  $P = 0.02$ . Forearm blood flow response to ACh improved ( $P < 0.001$ ), whereas SNP and L-NMMA responses were unchanged. A post-hoc colorimetric assay revealed in whole blood from healthy volunteers that pazopanib inhibited acetylcholinesterase activity by 35%.

**Conclusion:** Unexpectedly, pazopanib led to an increase in ACh response, but this is most likely due to the inhibition of acetylcholinesterase activity by pazopanib. Interestingly, we found that PVR was increased and capillary density reduced by the treatment, suggesting that capillary rarefaction could be one of the mechanisms behind VEGF inhibition induced hypertension.

### P30

#### A 12-WEEK EXERCISE TRAINING PROGRAM REDUCES ENDOTHELIAL DAMAGE IN RESISTANT HYPERTENSION

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**Background:** Resistant Hypertension (RH) is associated with an increased risk of cardiovascular events and poor prognosis. Exercise training studies in RH patients have shown promising outcomes, nonetheless, none determine the impact of exercise on endothelial damage and repair. Circulating endothelial cells (CECs) are a reliable indicator of vascular damage and dysfunction. Recent studies in hypertension suggest that increased levels of endothelial progenitor cells (EPCs), a marker of endothelial repair, are related to increased CECs in order to compensate endothelial damage. Purpose: This study aimed to determine the effect of 12-week aerobic exercise program on the percentage of EPCs and CECs in RH patients.

**Methods:** Patients with RH were randomized to a 12-week aerobic exercise program (3 xs/week) ( $n = 13$ ) and a usual care control group ( $n = 8$ ). Outcome measures included clinical data, ambulatory blood pressure data and circulating levels of EPCs, hematopoietic stem cells (HSC) and CECs, quantified by flow cytometry. (ClinicalTrials.gov: NCT03090529).

**Results:** Baseline characteristics were similar between groups, including the number of antihypertensive drugs ( $5.0 \pm 0.9$  vs.  $4.8 \pm 0.7$ ,  $p = 0.517$ ). After 12 weeks, no significant changes were found in the levels of HSCs in both groups. The levels of CECs decreased in the exercise group [0.0073

(0.0016)% to 0.0058 (0.0029),  $p = 0.019$ ]; no changes were observed in the control group. EPC's decreased only in the exercise group [0.0071 (0.0027)% to 0.0052 (0.0037)%],  $p = 0.046$ ].

**Conclusions:** Exercise training reduces endothelial injury/damage (reduced CECs levels) in RH patients, a specific group who is a challenge for clinicians as the available treatment options have reduced success.

### P31

#### DO TREATMENT INDUCED CHANGES IN ARTERIAL STIFFNESS AFFECT LEFT VENTRICULAR STRUCTURE AND FUNCTION? – A META-ANALYSIS

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**Background:** Vascular research demonstrated that pulse wave velocity (PWV), a measure of arterial stiffness, is inherently blood pressure-dependent. Considering the hypothesised pathophysiological chain of increased arterial stiffness leading to increased blood pressure load with consequent left ventricle hypertrophy (LVH) development, we conducted a systematic review of antihypertensive and lifestyle intervention studies to determine the association between on the one hand changes in arterial stiffness and blood pressure, and on the other hand changes in LV mass (LVM).

**Methods:** Using PubMed, EMBASE, Cochrane and Web of Science, we identified 23 studies, containing 2573 patients. Studies reported changes in arterial stiffness (assessed by means of PWV), systolic- and diastolic blood pressure (SBP, DBP), and LVM index (LVMI), respectively.

**Results:** Statistically significant reductions in SBP, PWV and LVMI were reported in 16, 14, and 20 studies, respectively. Pooled analysis of studies showed that the proportion in SBP reduction did not correlate significantly to the proportion in reductions of the other two variables. On the other hand, we found a significant positive correlation ( $r = 0.58$ ,  $p = 0.007$ ) between arterial stiffness and LVM regression, expressed as a relevant reduction in LVMI of 6.5 g/m<sup>2</sup> per 1.0 m/s reduction in PWV.

**Conclusions:** Our findings provide evidence that a decrease in arterial stiffness is associated with regression of LVH. To investigate whether there exists a causal relation between LVH due to arterial stiffness increases and in turn blood pressure load increases, future studies should strive for a multiple followup design and use of blood pressure-independent or -corrected stiffness indices.

### P32

#### DETERMINING CARDIAC AND ARTERIAL CONTRIBUTIONS TO CENTRAL PULSE PRESSURE

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We examined the ability of a simple reduced model comprising a proximal characteristic impedance linked to a Windkessel element to accurately predict central Pulse Pressure (PP) from aortic blood flow, verified that parameters of the model corresponded to physical properties, and applied the model to examine PP dependence on cardiac and vascular properties. PP obtained from the reduced model was compared with theoretical values obtained in silico and measured values in vivo. Theoretical values were obtained using a distributed multisegment model in a population of virtual (computed) subjects in which cardiovascular properties were varied over the pathophysiological range ( $n = 3,095$ ). In vivo measurements were in normotensive subjects during modulation of physiology with vasoactive drugs ( $n = 13$ ) and in hypertensive subjects ( $n = 156$ ). Central PP derived from the reduced model agreed with theoretical values (mean difference  $\pm$ SD,  $-0.09 \pm 1.96$  mmHg) and with measured values (means differences  $-1.95 \pm 3.74$  and  $-1.18 \pm 3.67$  mmHg for normotensive and hypertensive subjects, respectively). Parameters extracted from the reduced model agreed closely with theoretical and measured physical properties. Central PP was seen to be determined mainly by total arterial compliance (inversely associated with central arterial stiffness) and ventricular dynamics: the