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### **P32: DETERMINING CARDIAC AND ARTERIAL CONTRIBUTIONS TO CENTRAL PULSE PRESSURE**

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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

blood volume ejected by the ventricle into the aorta up to time of peak pressure and blood flow into the aorta (corresponding to the rate of ventricular ejection) up to this point. Increased flow and volume accounted for 20.1 mmHg (52%) of the 39.0 mmHg difference in PP between the upper and lower tertiles of the hypertensive subjects 1.

#### References

1. Vennin, S., Li, Y., Willemet, M., Fok, H., Gu, H., Charlton, P., Alastruey, J. and Chowiecnyk, P. (2017). Identifying Hemodynamic Determinants of Pulse Pressure: A Combined Numerical and physiological Approach. *Hypertension*, 70(6), 1176–1182.

#### Poster Session I – Hypertension II

##### P34

#### DETERMINANTS OF PERIPHERAL WAVE REFLECTION IN A LARGE TREATED HYPERTENSIVE POPULATION

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**Objective:** To evaluate the determinants of the peripheral wave reflection measured by the second derivative of the fingertip photoplethysmogram (SDPTG) among known cardiovascular (CV) risk factors in a large treated hypertensive population.

**Population and Methods:** We studied prospectively 316 hypertensive patients under treatment (154 male, mean age 54 yrs) by SDPTG automatically recorded from the second digit of the right hand (Fukuda FCP-3166<sup>®</sup>). The SDPTG waveform consisted of a, b, c and d waves in systole and e wave in diastole. The heights of the a, b and d waves were measured from the baseline, and d/a and b/a ratio were calculated. Augmentation index (AUI) was defined as the ratio of the height of the late systolic peak to that of the early systolic peak; SDPTG aging index (AGI) was calculated as (b-c-d-e)/a. The CV risk factors analyzed were systolic (SBP) and diastolic (DBP) blood pressure, heart rate (HR), left ventricle mass index (LVMI), creatinine, glycemia, cholesterol, triglycerides and body mass index (BMI).

**Results:** In the multivariate analysis the most significant associations were: AGI: age (+,  $p < 0,001$ ) and SBP (+,  $p < 0,05$ ); b/a: age(+,  $p < 0,001$ ), SBP(+,  $p < 0,01$ ) and HR(-,  $p < 0,01$ ); d/a: BP (-,  $p < 0,01$ ); AUI: SBP (+,  $p < 0,001$ ), HR (-,  $p < 0,001$ ) and BMI (-,  $p < 0,01$ ). When compared according BP control (<140/90 mmHg), AUI, b/a and d/a ratio were significantly higher in the patients whose BP was not controlled.

**Conclusion:** In treated hypertensives, changes in vascular wave reflection and stiffness were influenced by age, HR, and blood pressure control, most importantly SBP.

##### P35

#### ARTERIAL STIFFNESS AND CHRONIC STRESS: ROLE OF GENDER – RIGIDITÀ ARTERIOSA E STRESS CRONICO: RUOLO DEL GENERE

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**Aim:** Evaluate whether exposure to chronic stress is associated with early vascular aging in hypertensive patients and possible gender differences in this relationship.

**Methods:** Patients where recruited in a Hypertension outpatient clinic during a visit for the evaluation of subclinical organ damage. Aortic stiffness was measured as carotid-femoral pulse wave velocity (PWV) by applanation tonometry; common carotid intima-media thickness (IMT) and distensibility were evaluated by automated analysis of carotid ultrasound clips. Chronic stress was assessed using three different standardized scales: Perceived Stress Score 4 (PSS4), Depression Anxiety Stress Scale (DASS) and Chronic Stress Burden (CSB).

**Results:** Data from 125 patients (age  $56.7 \pm 12.5$  years) were analyzed. No significant differences were found between men and women in terms of PWV [8.90 (1.9) vs 8.55 (1.8) m/s,  $p = 0.14$ ], carotid distensibility ( $22.34 \pm 8.79$  vs  $21.17 \pm 8.74$  kPa<sup>-1</sup>,  $p = 0.545$ ) and IMT ( $0.74 \pm 0.12$  vs

$0.70 \pm 0.13$  mm,  $p = 0.132$ ). Women presented significantly higher scores of PSS4 (7(3) vs 5(3),  $p = 0.007$ ) and CSB ( $1.42 \pm 1.24$  vs  $0.59 \pm 0.85$ ,  $p = 0.004$ ). In the linear multiple regression analysis, CBS was correlated with PWV in the general population ( $\beta = 0.37$ ,  $p = 0.050$ ) being responsible for 4% of the variance of PWV, without significant gender differences. Among the components of CBS, difficulties in relationships with someone close to the participant were associated with increased PWV only in women ( $p = 0.01$ ). In a multiple regression model, this variable tended to be an independent predictor of PWV ( $\beta = 0.37$ ,  $p = 0.057$ ), responsible for 7% of the PWV variance.

**Conclusions:** In hypertensive patients, chronic stress burden is associated with greater arterial stiffness; in particular, stress related to difficulties in relationships seems to be associated with greater vascular stiffness only in women.

##### P36

#### PULSE WAVE VELOCITY (PWV) RESPONSES TO 3 MONTHS OF YOGA POSES AND RESPIRATORY CONTROL (UJJAYI PRANAYAMA) IN HYPERTENSIVE POST MENOPAUSE WOMEN: RANDOMIZED CLINICAL TRIAL

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**Background:** Non-pharmacological management of hypertension includes regular exercises. Yoga has been pointed as effective on treatment of hypertension. Its many aspects like yoga poses (asanas), respiratory control (pranayamas), meditation and others have not yet been assessed separately to understand its effects on cardiovascular issues. Thus, this study aims to partially clear the effects of yoga poses including exclusive muscle contraction known as bandhas (pelvic floor, core and throat), a specific respiratory technique ujjayi pranayama, whose translation is victory breath and active control group composed of stretching exercises on PWV.

**Methods:** Randomized trial assessing carotid femoral pulse wave velocity (cfPWV) by Complior<sup>®</sup>. Hypertensive post menopause women (HPMW) non-obese and non-smokers randomized in 4 groups (1- yoga poses + ujjayi; 2- yoga poses, 3- stretching exercises + ujjayi, 4- stretching exercises) attending 60 minutes assisted video classes twice a week (24 sessions). Data are presented as mean(M) ± standard error (SE). Generalized estimation equation (GEE) was used to data analysis,  $p \leq 0,05$ .

**Results:** 24 women recruited, randomized, 15 concluded study (1- n=3; 2- n=6; 3- n=4; 4- n=2). Group 1 showed cfPWV at 10,  $0 \pm 0, 23$  m/s; 2-  $8,9 \pm 0,29$  m/s; 3-  $7,7 \pm 0,53$  m/s; 4-  $8,8 \pm 0,24$  m/s at baseline. Post intervention presented 1-  $-1,8 \pm 0,31$  m/s  $p = 0,00$ ; 2-  $-0,43 \pm 0,25$  m/s  $p = 0,08$ ; 3-  $-1,4 \pm 0,27$  m/s  $p = 0,00$ ; 4-  $1,4 \pm 0,99$  m/s  $p = 0,16$ .

**Conclusion:** The present study has demonstrated an effect of respiratory control ujjayi pranayama on cfPWV after 3 months in HPMW.

##### P37

#### PULSE WAVE VELOCITY: DEPENDENCE ON CONTEMPORANEOUS AND HISTORICAL BLOOD PRESSURE COMPONENTS

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**Background:** Arterial stiffness as measured by PWV along the aorta is an important determinant of cardiovascular risk. PWV is known to be dependent on contemporaneous blood pressure (BP) but its dependence on long-term BP has not been established.

**Methods:** Subjects from Twins UK who had tonometric measures of carotid-femoral PWV with previous longitudinal measures of blood pressure ( $n = 2094$ ) and, in a sub-sample, PWV ( $n = 956$ ) were studied. Brachial artery pulse pressure (PP) and mean arterial pressure (MAP) were averaged over the period of longitudinal follow-up to obtain measures of historical PP and MAP (PPH and MAPH). The relationship of PWV to contemporaneous PP and MAP (PPC and MAPC) was compared with that to PPH and MAPH.

**Results:** The average duration of blood pressure measurement was  $14.0 \pm 4.3$  years. PWV correlated strongly with PPC ( $r = 0.542$ ,  $p < 0.001$ ), PPH ( $r = 0.474$ ,  $p < 0.001$ ), MAPC ( $r = 0.462$ ,  $p < 0.001$ ) and MAPH ( $r = 0.360$ ,  $p < 0.001$ ). In multiple regression analysis incorporating