



## Artery Research

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### **PO-20: A HYDROGEN SULFIDE PRODRUG AUGMENTS ANGIOGENESIS IN A SWINE MODEL OF CRITICAL LIMB ISCHEMIA VIA A NITRIC OXIDE DEPENDENT MECHANISM**

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(BPV) and baroreceptor sensitivity (BRS) can provide insight into aspects of autonomic function, particularly following an aerobic exercise bout.

**Purpose:** To examine BPV and BRS in normotensive obese individuals in response to aerobic exercise.

**Methods:** Normal-weight (n=8; 25 yr; 23.0 kg/m<sup>2</sup>) and obese individuals (n=9; 27 yrs; 32.2 kg/m<sup>2</sup>) performed a 60-min leg cycling exercise at 60% of VO<sub>2peak</sub>. Beat-by-beat blood pressure was recorded at baseline, immediately post-exercise and 30 min into passive recovery using finger plethysmography. R-R intervals were obtained at 1,000 Hz with a digital acquisition system. Power spectral analysis was conducted using WinCPRS software for estimates of BPV (very low and low frequency (VLF, LF), and systolic and diastolic deviation (SDev, DDev)). BRS was estimated using the sequence technique. Natural log-transformed was performed on LF BPV (LnLF) to account for non-normal distribution.

**Results:** HR increased from baseline similarly in both groups (p<0.05). The control group decreased SBP at immediately post-exercise compared to baseline measurements (p<0.05), but not the obese group. A main effect of time and group (p<0.05) existed for BRS. No group differences were found on DBP, LF, LnLF, VLF, SDev and DDev.

**Conclusion:** The results showed no difference in the BPV indices between the obese and control groups. The different response in SBP suggests that control group may have better BRS; however, this is not supported by the lower values in BRS. A limitation of this study may be the small number of participants.

**Conclusions:** These data suggest that NO contributes to  $\beta_2$ -adrenergic mediated vasodilation in young premenopausal women. In contrast, no contribution of NO to  $\beta_2$  mediated vasodilation was observed in PM women. These data suggest a lower  $\beta_2$ -adrenergic responsiveness in PM women may be due to a reduced contribution of NO.

#### PO-19 ASSOCIATIONS OF WALKING WITH SARCOPENIC OBESITY AND CARDIOVASCULAR DISEASE RISK FACTORS IN OLDER ADULTS

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**Objectives:** To investigate the associations of walking (steps/day) with sarcopenic obesity (SO) and cardiovascular disease (CVD) risk factors in older adults.

**Methods:** This cross-sectional study included 297 older adults aged  $\geq 65$  years (mean age 72, ranged 65-95). Walking was assessed using an accelerometer (Omron HJ-321) and categorized into thirds (tertile) based on the average daily steps. SO was defined based on physical function (gait speed), muscle strength (handgrip strength), and muscle mass (appendicular lean mass [ALM] index) according to the Foundation for the National Institutes of Health Sarcopenia Project diagnostic criteria, and % body fat (obesity as  $\geq 25\%$  in men and  $\geq 30\%$  in women) using Dual Energy X-Ray absorptiometry.

**Results:** Each 10,000 steps/day increase was associated with improved SO

	Control			Obese		
	Baseline	Immediate	30min	Baseline	Immediate	30min
HR (bpm)*	66 ± 11	88 ± 12	80 ± 12	60 ± 6	79 ± 11	74 ± 11
SBP (mmHg)**&	116 ± 11	104 ± 8 <sup>abc</sup>	115 ± 9	122 ± 5	119 ± 6	122 ± 4
DBP (mmHg)	64 ± 10	64 ± 4	68 ± 7	69 ± 5	71 ± 5	72 ± 5
Raw LF (mmHg2)	9.00 ± 5.37	15.91 ± 15.03	15.24 ± 12.29	5.23 ± 4.65	6.89 ± 4.93	9.64 ± 8.13
LnLF (mmHg2)	2.07 ± 0.53	2.40 ± 0.89	2.41 ± 0.89	1.37 ± 0.75	1.73 ± 0.66	1.89 ± 0.98
VLF (mmHg2)	20.83 ± 14.39	29.63 ± 19.77	22.69 ± 13.67	11.91 ± 7.96	18.68 ± 14.70	15.29 ± 10.87
BRS (ms/mmHg)**	15.95 ± 7.92	5.20 ± 3.48	8.05 ± 4.52	19.38 ± 6.79	12.74 ± 8.70	14.49 ± 7.79
SDev (mmHg)	5.61 ± 1.75	7.14 ± 2.71	6.36 ± 2.25	4.77 ± 1.48	5.83 ± 2.42	5.50 ± 2.02
DDev (mmHg)	3.70 ± 1.08	4.06 ± 1.56	3.84 ± 3.1	3.67 ± 1.33	4.18 ± 1.67	3.90 ± 1.30

All data are mean ± SEM. \*Time effect, # Group effect, & time x group effect, a Within-Subjects effect vs Baseline, b Within-Subjects effect vs 30min, c Between-Subject effect vs obese group.

#### PO-17 ROLE OF NITRIC OXIDE IN $\beta_2$ -ADRENERGIC MEDIATED VASODILATION IN POSTMENOPAUSAL WOMEN

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**Objectives:** Postmenopausal (PM) women have a blunted  $\beta_2$ -adrenergic receptor-mediated responsiveness when compared to young premenopausal women in part due to a reduction in the relative contribution of nitric oxide (NO) to  $\beta_2$ -adrenergic mediated vasodilation. Hence, we tested the contribution of NO to  $\beta_2$ -adrenergic receptor-mediated vasodilation during terbutaline infusion.

**Hypothesis:** We hypothesized that the contribution of NO to  $\beta_2$ -adrenergic mediated vasodilation would be attenuated in PM women as compared to young women.

**Methods:** Venous occlusion plethysmography was used to measure forearm blood flow (FBF) in 7 healthy young premenopausal women and 9 healthy PM women (mean age = 27 ± 1 and 60 ± 1 years, respectively). FBF was measured at baseline and during terbutaline infusion at 0.1, 0.5, 1.0, 2.0  $\mu\text{g}/100\text{ml}$  tissue/min before (with saline co-infusion) and during NO synthase inhibition with L-NMMA. Forearm vascular conductance was calculated from FBF and mean arterial pressure.

**Results:** In young women, there was a significant L-NMMA effect on forearm vascular conductance during terbutaline infusion with and without L-NMMA (1.7 ± 0.14, 3.56 ± 0.41, 7.13 ± 1.11, 7.87 ± 0.74, 10.54 ± 1.81 versus 2.08 ± 0.28, 5.54 ± 0.50, 9.32 ± 1.10, 10.77 ± 1.49, 13.29 ± 1.94 ml/100ml tissue/min/mmHg, respectively). However, there was no effect of L-NMMA in PM women during terbutaline infusion with and without L-NMMA (1.34 ± 0.26, 2.37 ± 0.32, 5.21 ± 0.99, 4.71 ± 0.99, 6.43 ± 1.37 versus 1.62 ± 0.31, 3.11 ± 0.55, 5.41 ± 1.12, 6.26 ± 1.38, 7.26 ± 1.44 ml/100ml tissue/min/mmHg, respectively).

variables and CVD risk factors, specifically with 0.008 faster gait speed (m/s), 0.006 higher muscle mass index (ALM/BMI), 0.59 lower % body fat (%), and 0.68 lower fasting glucose (mg/dl)(all p < 0.05) in the linear regression after adjusting for age, sex, smoking status, and alcohol intake. Compared to low walking group, odds ratios (ORs)(95% confidence intervals [95% CIs]) in moderate and high walking groups were 0.18 (0.02-1.54) and 0.22 (0.03-2.01) for slow walking, 0.42 (0.14-1.30) and 0.34 (0.09-1.29) for weak handgrip strength, 0.45 (0.23-0.87) and 0.44 (0.22-0.88) for low muscle mass, 0.58 (0.13-2.57) and 0.46 (0.11-2.06) for high % body fat, and 0.62 (0.17-2.28) and 0.21 (0.02-1.78) for SO, respectively, in the multivariable logistic regressions. Compared to individuals without SO, ORs (95% CIs) in individuals with SO were 2.04 (0.58-7.18) for hypertension, 1.27 (0.39-4.22) for hypercholesterolemia, and 1.87 (0.37-9.45) for type 2 diabetes in the multivariable logistic regression. However, these associations appeared to be weaker after further adjustment for walking (steps/day).

**Conclusion:** This study suggests that walking in older adults is associated with lower risks of SO and CVD risk factors.

#### PO-20 A HYDROGEN SULFIDE PRODRUG AUGMENTS ANGIOGENESIS IN A SWINE MODEL OF CRITICAL LIMB ISCHEMIA VIA A NITRIC OXIDE DEPENDENT MECHANISM

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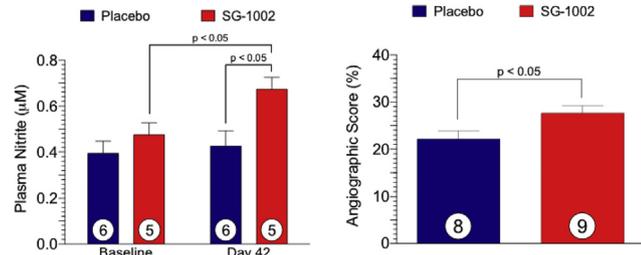
**Introduction:** Despite advances in revascularization, treatments for critical limb ischemia (CLI) have been largely unsuccessful. Hydrogen sulfide (H<sub>2</sub>S)

and nitric oxide (NO), are endogenous gasotransmitters which exert potent vasodilatory and proangiogenic effects. Recent experimental evidence suggest that the proangiogenic effects of H<sub>2</sub>S are mediated in part through the NO pathway. We sought to determine whether a novel H<sub>2</sub>S prodrug, SG-1002 (Sulfagenix, Inc. Cleveland OH), increases NO production and promotes peripheral revascularization.

**Methods:** CLI was generated in Yucatan miniswine (n=17) via carotid cut-down and placement of an Amplatzer vascular plug deployed within a Via-bahn stent positioned proximally in the external iliac artery. At day 7 post-CLI pigs, received daily placebo or SG-1002 (1600 mg PO). Cuff-p pressures were measured weekly by ankle/brachial index (ABI). Plasma H<sub>2</sub>S, H<sub>2</sub>S metabolite sulfane sulfur (SS), and NO metabolite, nitrite (NO<sub>2</sub>) were measured. At day 42 post-CLI, digital subtraction angiography (DSA) was performed and opacified vessels quantitated.

**Results:** ABI was reduced to 0 following CLI induction. ABI improved in both groups but continued to demonstrate persistent ischemia with values below 0.25 at day 42 and showed no difference between groups. Circulating H<sub>2</sub>S levels were similar between groups. SS levels were increased from baseline to day 42 in SG-1002 treated pigs (p < 0.001) but remained unchanged in placebo treated animals. At day 42, SG-1002 treatment increase circulating NO<sub>2</sub> levels (p < 0.05) compared to placebo. There was an increase in NO<sub>2</sub> levels from baseline to day 42 in SG-1002 treated pigs (p < 0.05). DSA revealed an increase of CLI limb vessel number in SG-1002 treated pigs compared to placebo (p < 0.05).

**Conclusions:** Treatment with the H<sub>2</sub>S prodrug, SG-1002, results in increased metabolites of H<sub>2</sub>S and NO signaling. H<sub>2</sub>S treatment increased vascular density in the setting of severe CLI in a clinical relevant swine model.



## PO-22

### BODY MASS INDEX AS AN INDEPENDENT PREDICTOR OF CHANGE IN ARTERIAL STIFFNESS PARAMETERS WITH CHANGE IN BODY POSITION

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Changing from supine to a seated position creates an orthostatic challenge due to the effects of gravity on the distribution of blood. This redistribution of volume unloads baroreceptors and may evoke sympathetic activation. The sympathetic activation may lead to increases in arterial stiffness, but it is unknown as to how different demographic variables may impact these changes.

**Objective:** To investigate whether the change in arterial stiffness parameters between two positions is influenced by factors such as age, sex, or body mass index (BMI).

**Methods:** Thirty healthy, young adults (24±4 years) were randomly positioned supine or semi-supine, at two different angles (0°, 72°) on an adjustable table. After 5 minutes rest, arterial stiffness parameters of the common carotid artery were obtained via ultrasound: beta stiffness index, elastic modulus (Ep), arterial compliance (AC), and distensibility, as well as cardio-ankle vascular index (CAVI) from the VaSera (Fukuda Denshi, Tokyo, Japan). Linear regression was used on the change value for each arterial stiffness parameter adjusting for age, sex, BMI, and baseline values of each outcome measure.

**Results:** BMI was a significant independent predictor of changes in each measured arterial stiffness parameter after controlling for age and sex. Increasing BMI is related to greater changes in beta stiffness ( $\beta=0.55, p=0.001$ ) and Ep ( $\beta=0.58, p=0.001$ ) with change in position. Concomitantly, increasing BMI is associated with smaller changes in AC ( $\beta=-0.31, p=0.03$ ), distensibility ( $\beta=-0.54, p=0.001$ ), and CAVI ( $\beta=-$

0.48,  $p=0.001$ ). Sex was only a significant independent predictor when assessing change in CAVI ( $\beta=-0.44, p=0.001$ ).

**Conclusion:** When measuring arterial stiffness parameters in different positions, it is important to account for the effect of BMI in the analyses. Although obesity is associated with increased baseline sympathetic activity and reduced baroreceptor sensitivity, the change in position creates a larger change in arterial stiffness which may relate to the greater displacement of blood volume with a larger body size.

## PO-23

### A SYSTEMATIC REVIEW ON THE EFFECT OF ACUTE AEROBIC EXERCISE ON ARTERIAL STIFFNESS REVEALS A DIFFERENTIAL RESPONSE IN THE UPPER AND LOWER ARTERIAL SEGMENTS

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**Objectives:** The overall impact of resistance-type exercises and chronic physical activity on the modulation of arterial stiffness has been well characterized; however, the impact of acute aerobic exercise remains unclear. Therefore, we aimed to synthesize evidence pertaining to acute changes in arterial stiffness shortly following aerobic exercise in healthy individuals.

**Methods:** Electronic databases (MEDLine, EMBASE, Cochrane Library, Sport Discus, and Web of Science) were searched to identify articles assessing the effects of acute aerobic exercise on parameters of arterial stiffness. Eligible studies included arterial stiffness measurements before and after acute exercise in healthy adults, who were free of any cardiovascular risk factors, and were not taking cardioprotective medications.

**Results:** A total of 43 studies were included. The effect of acute aerobic exercise on arterial stiffness was found to be dependent on the anatomical segment assessed, and on the time at which the measurement was performed post-exercise. Arterial stiffness of the *central and upper body peripheral arterial segments* was found to be increased relative to resting values immediately post-exercise (0-5 minutes), while thereafter (>5 minutes) was decreased to a level at, or below resting values. In the *lower limbs*, proximal to the primary working muscles, arterial stiffness decreased immediately post-exercise (0-5 minutes), which persisted into the recovery period post-exercise (>5 minutes).

**Conclusions:** This systematic review reveals a differential response to acute exercise in the lower and upper/central arterial segments in healthy adult subjects. We further showed that the effect of acute exercise on arterial stiffness is dependent on the time at which the measurement is performed following acute aerobic exercise. Therefore, when assessing the overall impact of exercise on arterial stiffness it is important to consider the arterial segment being analysed and the measurement time point, as failure to contextualize the measurement can lead to conflicting results and misleading clinical inferences.

## PO-24

### RELATIONSHIP BETWEEN STEP COUNTS AND CAROTID FEMORAL PULSE WAVE VELOCITY IN ADULTS TREATED FOR HYPERTENSION AND DIABETES

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**Objectives:** 'Step counts' captured by wearable physical activity tracking devices are associated with reductions in cardiovascular disease. However, in individuals on cardioprotective medications the impact of step counts may not be captured by the measurement of traditional cardiometabolic