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Effects Of Eccentric Cycling On Blood Flow Patterns And Vascular Reactivity

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EFFECTS OF ECCENTRIC CYCLING ON BLOOD FLOW PATTERNS AND VASCULAR
REACTIVITY

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Manuel Gomez

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EFFECTS OF ECCENTRIC CYCLING EXERCISE ON BLOOD FLOW PATTERNS AND
VASCULAR REACTIVITY

by

MANUEL GOMEZ, BS

THESIS

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Table of Contents

Table of Contents	iv
List of Tables	v
List of Figures	vi
Introduction.....	1
Cardiovascular Disease	1
Exercise.....	2
Eccentric Exercise.....	4
Hypothesis.....	6
Methods.....	7
Research Design.....	7
Endothelial Shear Stress	10
Blood Flow Patterns.....	11
Statistical Analysis.....	12
Results.....	12
Descriptives.....	12
Data normality	14
Endothelial Shear Stress and Blood Flow Patterns Results	15
Flow Mediated Dilatation and Venous Occlusion Plethysmography Results	21
Discussion	28
Limitations	31
Conclusion	31
References.....	32
Vita.....	39

List of Tables

Table 1	12
Table 2. Descriptive data are represented in mean, sd, and standard error of the mean in Table 2 for all the participants and grouped by Sex (Female and Male) during eccentric exercise on visit 2.....	13
Table 3. Pairwise comparisons and Effect Size between exercise intensities on antegrade ESS. 15	
Table 4. Pairwise comparisons and Effect Size between exercise intensities on ESS retrograde. 16	
Table 5. Pairwise comparisons and Effect Size between exercise intensities on antegrade RE... 18	
Table 6. Pairwise comparisons and Effect Size between exercise intensities on retrograde RE.. 19	
Table 7. T test or Wilcoxon test for pre to post differences with Hedge's g or Wilcoxon's effect size.	21
Table 8. FMD pre and post, baseline, peak and difference.....	27

List of Figures

Figure 1. Exercise-induced improvement leads to increased endothelial perfusion (Ghisi et al., 2010).	3
Figure 2. First visit protocol.....	8
Figure 3. Second visit	9
Figure 4 Visit	11
Figure 5. ESS antegrade for all intensities.	15
Figure 6. ESS Antegrade between intensities and sex.	16
Figure 7. ESS retrograde for all intensities.	17
Figure 8. ESS retrograde between intensities and sex.	17
Figure 9. Reynolds number antegrade by intensity.	18
Figure 10. Reynolds number anterograde by intensity and sex.	19
Figure 11. Reynolds number retrograde by intensitiy.....	20
Figure 12. Reynolds number retrograde by intensity and sex,	20
Figure 13. FMD pre to post.....	21
Figure 14. Upper basal.....	22
Figure 15. Upper ischemia.....	22
Figure 16. Upper postischemia.	23
Figure 17. Lower basal.	23
Figure 18. Lower ischemia.	24
Figure 19. Lower extremity postischemia.	24
Figure 20. FMD pre and post peak.	25
Figure 21. FMD pre and post difference.....	25
Figure 22. FMD pre and post basal measurement.	26

Introduction

CARDIOVASCULAR DISEASE

In 2020, approximately 19 million deaths were attributed to cardiovascular disease (CVD) globally, which amounted to an increase of 18.7% from 2010 (Tsao et al., 2022). CVD in the United States costs about \$363 billion each year from 2016 to 2017 (Virani et al., 2021). Endothelial dysfunction, which is characterized by a decrease in nitric oxide (NO) bioavailability, is the first pathophysiological step for atherosclerosis, which causes 90% of CVD. However, endothelial shear stress is the primary physiological stimulus to enhance endothelial function. Due to the increase in oxidative stress, the endothelial NO synthase (the enzyme that produces NO) is uncoupled, therefore leading to a decrease in NO production and bioavailability (Libby et al., 2002). This chain of events correlates with endothelial dysfunction, unfolding atherosclerosis. Atherosclerosis is a pathological deterioration of endothelium that results in vessel blockage (Flammer et al., 2012; Ratcliffe et al., 2017) (Ratcliffe et al., 2017). Several studies have demonstrated the association between abnormal endothelial function and cardiovascular diseases, considering endothelial dysfunction as the triggering factor of the atherogenesis process (Ghisi et al., 2010). The vascular endothelium is responsible for the synthesis of vasoconstrictor and vasodilating factors, which NO being one of the most important endothelial-derived relaxation factors (Ghisi et al., 2010; Goto et al., 2003; Leung et al., 2008; Vanhoutte et al., 2009).

The decrease in the bioavailability of NO endothelial dysfunction seems to be present in the CVD (Allen et al., 2006; Ghisi et al., 2010).

Insufficient physical activity is a key factor for CVD. It is known that moderate exercises are stimulators of NO release, therefore regular physical exercise can be considered a protective

factor against CVD (Ghisi et al., 2010) (Manson et al., 2002) (Hambrecht et al., 2000). Evidence supports the protective effect of exercise on the decrease of oxidative stress, which has a direct impact on the use of exercise practice as a treatment of cardiovascular disease (Ghisi et al., 2010; Hamburg et al., 2007; Leung et al., 2008; Vanhoutte et al., 2009).

EXERCISE

Exercise has been demonstrated to reduce the risk of CVD, and the health benefits of regular physical activity are irrefutable (Warburton & Bredin, 2016). Even low physical activity loads below the minimum World Health Organization (WHO) recommendations can provide major benefits, such as improved cardiometabolic biomarkers in adolescents (Warburton & Bredin, 2016) or reduced all-cause mortality in adults (Ekelund et al., 2015; Zhao et al., 2014). The promotion of regular physical activity worldwide is needed to decrease the substantial global economic burden (including direct health-care costs, productivity losses, and reductions in disability-adjusted life years) attributable to physical activity (Fiuza-Luces et al., 2018). In addition, exercise is directly correlated with endothelial function and NO bioavailability. Studies by Oldridge (Ghisi et al., 2010; Oldridge et al., 1988) and O'Conner (Ghisi et al., 2010; O'Connor et al., 1989) confirmed a decrease of 20% to 25% in the mortality due to cardiovascular disease in patients submitted to cardiac rehabilitation. As well as a study containing 3,000 healthy men and women in the USA showed the association between the regulatory effect of physical activity on inflammation and the decrease in the risk of cardiovascular events (Abramson & Vaccarino, 2002; Ghisi et al., 2010). The beneficial effects of the regular practice of exercise on CVD are especially associated with the higher production of vasodilating agents derived from the vascular endothelium, with the consequent decrease in peripheral resistance (Figure 1) (Ghisi et al., 2010; Kingwell, 2000).

Higashi studied blood flow in the forearm with a 12-week program of physical exercises, the blood flow response in the forearm of the physical training group significantly increased when compared to the control group (Ghisi et al., 2010; Higashi et al., 1999). As well as DeSouza, found a significant increase in blood flow of the forearm comparing young individuals, middle-aged adults, and elderly individuals that were endurance runners (DeSouza et al., 2000; Ghisi et al., 2010).

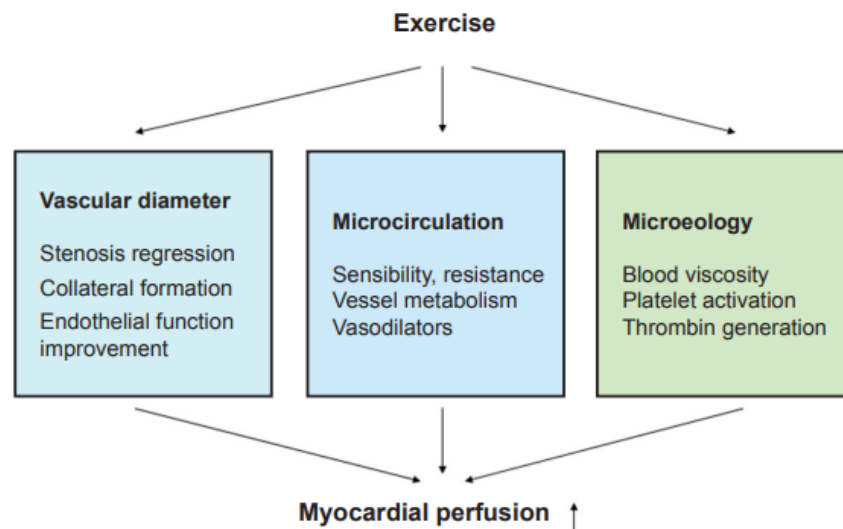


Figure 1. Exercise-induced improvement leads to increased endothelial perfusion (Ghisi et al., 2010).

Gurovich and Braith (2013), and Morales-Acuna et al. (2019) evaluated blood flow patterns created by enhanced external counterpulsation and its effects on femoral and brachial FMD in 18 healthy young males. It was found that enhanced external counterpulsation generated retrograde turbulent blood flow in the femoral artery and this blood flow pattern improved femoral FMD (Morales-Acuna et al., 2019). As well as Gurovich and Braith (2013), and Morales-Acuna et al. (2019) analyzed blood flow patterns in the brachial and femoral arteries during endurance and resistance exercise of eight young healthy males and described the

presence of turbulence blood flow when workloads were 49% or above their maximal exertional capacities during both types of exercises. The beneficial effects of exercise on vascular health are well established (Green et al., 2017; Morales-Acuna et al., 2019), and the fact that turbulence may also be favorable for the vasculature.

Even though exercise contributes enormously to the prevention of CVD, there are populations that due to its high metabolic and physical demands, traditional exercise is not a viable option. Therefore, the next route for these types of populations suffering from CVD and other respiratory complications is eccentric exercise.

ECCENTRIC EXERCISE

Eccentric exercise has been proposed as an alternative form of exercise for certain clinical populations including older populations, which have been to improve health and fitness parameters with eccentric exercise (González-Bartholin et al., 2019). As well as those cardiac and pulmonary patients who may not tolerate high-intensity exercise (Peñailillo et al., 2014).

Eccentric exercise is characterized by a muscle contraction while the muscle is increasing its length. Many daily activities use eccentric contractions such as walking downstairs or sitting down, including exercises in downhill running or walking (Chen et al., 2008) as well as the lengthening phase of resistance exercises (Chen et al., 2010; Hortobágyi et al., 1996). Eccentric cycling was first introduced by Abbot in 1952, while technology was not advanced, the idea was there. Abbot used two bicycles with one person pedaling forward and the other resisting the backward movement (Abbott et al., 1952). As introduced by Abbot in 1952, eccentric exercise had a lower metabolic cost compared directly to concentric exercise (Abbott et al., 1952). Abbot reported oxygen consumption (VO_2) was 41%, 49%, and 66% lower during eccentric pedaling performed at 25, 35, and 52 rpm respectively when compared with concentric cycling at

intensities ranging between 24W and 245W. Other researchers confirmed similar findings showing that eccentric cycling requires only 25%-30% of the oxygen required for concentric cycling at the same workload (Knuttgén et al., 1982; Perrey et al., 2001). Peñailillo et al. also concurs with similar findings that eccentric cycling was less metabolically demanding than concentric cycling by 50% (Peñailillo et al., 2013). A study conducted by Peñailillo et al. explains that a study by Bigland- Ritchie, and Woods reported that muscle consumed 79% less oxygen in eccentric than concentric cycling for the same work output, speculated that this was due to fewer muscle fibers being recruited to perform eccentric versus concentric cycling.

To the best of our knowledge, there is a gap in the literature comparing blood flow patterns at different intensities during eccentric exercise. As well as a direct comparison of metabolic cost differences between concentric and eccentric cycling per cycling intensity.

To the best of our knowledge, there is a gap in the literature comparing blood flow patterns at different intensities during eccentric exercise. As well as a direct comparison of metabolic cost differences between concentric and eccentric cycling per cycling intensity.

Hypothesis

Hypothesis 1 – Blood flow patterns and endothelial shear stress during eccentric cycle exercise will be higher at a high intensity than at moderate and lower intensities, and baseline.

Hypothesis 2- Endothelial function, measured via flow mediated dilation (FMD) and venous occlusion plethysmography (VOP) will increase post-exercise when compared to baseline after a 30-minute eccentric cycle exercise.

Methods

RESEARCH DESIGN

A convenience sample of college students was recruited from The University of Texas at El Paso and its surroundings. Inclusion and exclusion criteria defined that the subjects are apparently healthy, normotensive, non-smokers, have no known cardiovascular or cardiac disease, take no prescribed medications, excluding birth control, no over-the-counter medications such as acetaminophen or nonsteroidal anti-inflammatories (NSAIDs), have no injury that would affect exercise or ultrasound imaging, and take no nutritional supplements containing antioxidants. All subjects completed visits in the morning to avoid any diurnal changes. Females were assessed within a period that spanned four days before to four days after menses to reduce any hormonal influence on vascular reactivity (Adkisson et al., 2010; Mattu et al., 2020). All individual participants included in the study signed an informed consent approved by UTEP's IRB before scheduling the first visit to the Clinical Applied Physiology (CAPH) lab.

During the first lab visit (figure 2), an assessment of weight (WB-110A Class III, Tanita, Japan), height (Seca Medical, Germany), and body mass index (BMI) was performed.

Subjects sat down at the cycle ergometer (Corival, Lode) and performed a graded exercise test (GXT) to determine maximal oxygen consumption (VO_2max) (TrueOne 2400, Parvomedics Inc.) and peak power. Seat height was adjusted to allow knee flexion of approximately 5 to 15 degrees during cycling. The GXT was a multistage incremental stage starting at 50 watts and increasing 50 watts for males and 25 watts for females, every two minutes until exhaustion, lasting approximately 8-12 minutes. Heart rate (HR), rate of perceived exertion (RPE), Blood lactate (m/mmol) (Lactate Plus, Nova Inc.), and power output (PO) at the end of each stage. Blood lactate samples were obtained by earlobe micro-puncture. After the GXT on the first visit, a five-minute

familiarization stage was implemented on an eccentric bicycle (Grucox Medical (Pty) Ltd., South Africa) at 60rpm, and 100 watts torque.

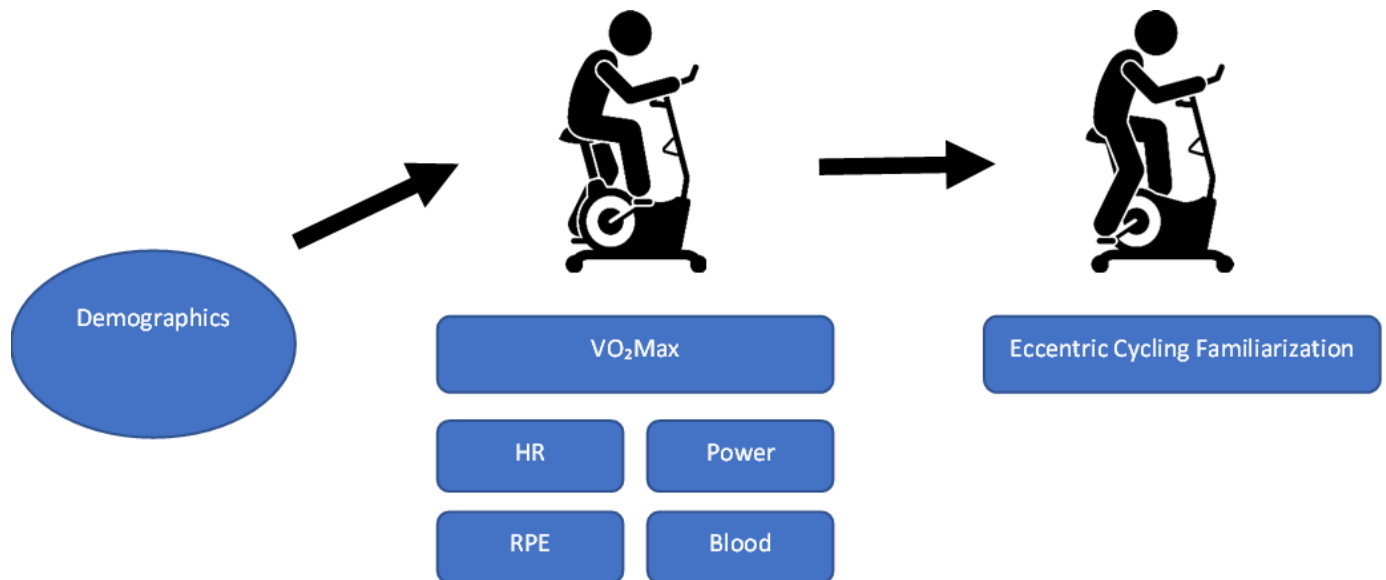


Figure 2. First visit protocol

Second visit (Figure 3) 48-hr after the first visit on an eccentric bicycle three workloads were determined based on the observed power at different lactate levels from the GXT (low intensity: 0-2 mmol/L; moderate: 2-4 mmol/L; and high: >4 mmol/L). The eccentric bicycle was set up at 60rpm and the respective power in watts. Subjects had to make resistance and sustain cadence to fulfill the watts needed to meet the intensity regimen. Subjects pedaled for 3-5 minutes then at the end of each stage, blood flow patterns were determined by high-definition ultrasound and Doppler on the brachial artery, as previously reported (Alvaro N. Gurovich et al., 2021; A. N. Gurovich et al., 2021; Morales-Acuna et al., 2019). Test subjects were instructed to keep their right arm straight on a tripod for imaging and recording of ultrasound video (MyLab30 Gold Cardiovascular, Esaote). Blood flow patterns and brachial artery diameters (intima to intima) via Doppler (2-mm window placed in the middle of the artery following the

longitudinal axis) were recorded using a Brachial artery analyzer (MIA, Iowa, and more). HR, RPE, and lactate was recorded as well at the end of each stage.

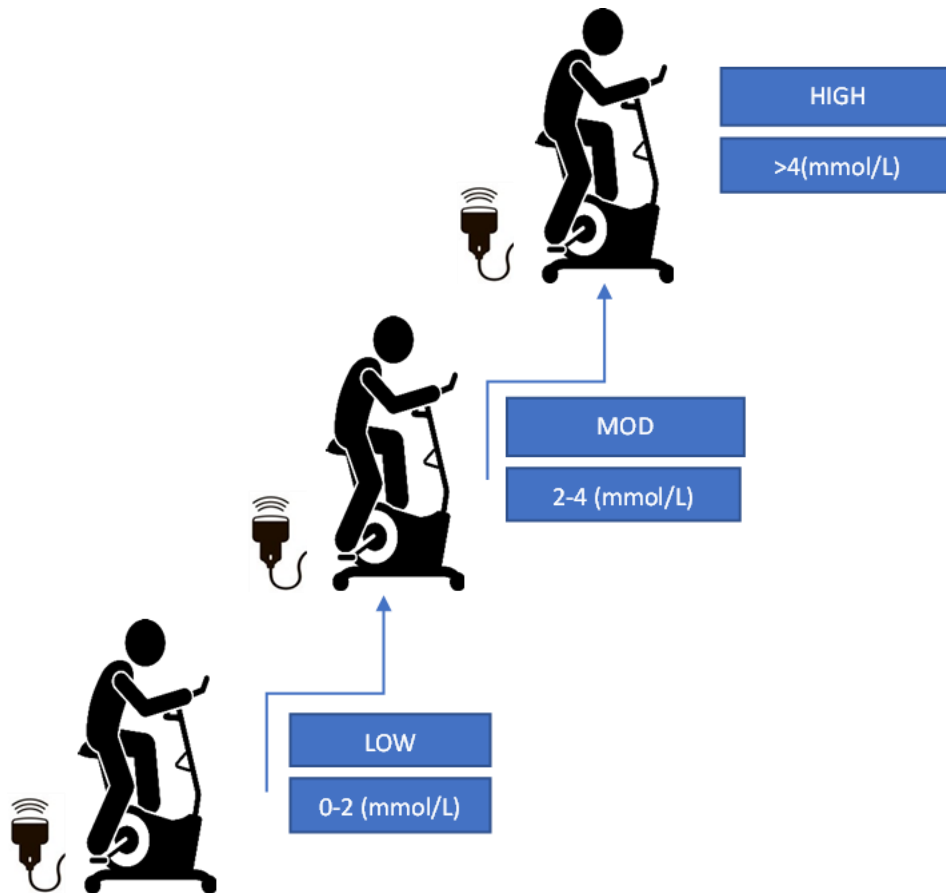


Figure 3. Second visit

Third visit (Figure 4) to the laboratory 48 hours after visit two, the subject laid in a supine position on a medical bed, for ten minutes after arrival, to acquire accurate basal measurements. After 10 minutes, blood pressure was taken three times to verify subject basal was established. VOP and FMD were performed simultaneously, right extremities for VOP and the left arm for FMD. VOP used the right forearm and right calf using a validated plethysmograph (AI6, Hokanson, Bellevue, WA). Pressure cuffs were placed at the bicep, wrist, thigh, and at the ankle. Strain gauges were placed at the largest perimeter of both the calf and forearm. VOP data was collected during resting

and post-5-min ischemic stress conditions. During FMD measurements, a total of six electrodes were attached to their chest in the standard lead II setting, three electrodes were connected to a high-definition ultrasound machine (MyLab30 Gold Cardiovascular, Esaote, Firenze, Italy) and the other three were connected to an electrocardiogram trigger system (MP150WSW, BIOPAC Systems Inc., Goleta, CA and Frame Grabbing and Digital Data Input modules, Medical Imaging Applications LLC, Coralville IA). Then, the right arm was placed at 80 -90° of shoulder abduction over an armrest and a blood pressure cuff was attached to the forearm, just below the antecubital fossa. A 12 -MHz linear phase array ultrasound transducer (LA435, Esaote, Firenze, Italy) was placed 5 cm above the antecubital fossa which was used to image the right brachial artery following international guidelines for FMD (Corretti et al., 2002; Harris et al., 2010). Basal artery diameters and peak systolic blood flow velocities were recorded in basal conditions for 30 seconds using an automated edge-detection software (Vascular Research Tools, Medical Imaging Applications LLC) at every QRS complex captured by the electrocardiogram trigger system. Then, the forearm cuff was inflated to supra systolic pressure (>200 mmHg) for 5 minutes followed by the deflation of the cuff. Artery diameters and blood flow velocities were continuously registered every 3 seconds for 150 seconds, starting at 30 seconds before deflation until 2 minutes after deflation using the automated edge-detection software. Peak diameters were identified as the single peak diameter observed during the plateau phase after cuff deflation (Sonka et al., 2002). The reliability of FMD analysis in our lab has already been tested and is described elsewhere (Ratcliffe et al., 2017). FMD will be calculated as $FMD \% = 100 \times (\text{peak diameter} - \text{basal diameter}) / \text{basal diameter}$, FMD absolute difference = peak diameter – basal diameter, and allometric FMD = $100 \times (\text{peak diameter} / \text{basal diameter}^{0.98})$ (Atkinson et al., 2013; Morales-Acuna et al., 2019).

ENDOTHELIAL SHEAR STRESS

Endothelial shear stress (ESS) was estimated every 3 seconds by Womersley's approximation, using $ESS = \mu * SR$ and $SR = 2 K * V/D$, where μ is blood viscosity, SR is shear rate, V is peak

systolic velocity, D is artery diameter, K is a complex factor dependent only on the Womersley parameter (α), and $\alpha=(D/2)*(\omega/(\mu/\rho))^{1/2}$, where ω is the angular frequency of the flow pulsation ($\omega=freq*2\pi$), ρ is blood density, and μ is blood viscosity (Morales-Acuna et al., 2019; Parker et al., 2009; Simon et al., 1990). ESS was expressed in dynes/cm². (Morales-Acuna et al., 2019)

BLOOD FLOW PATTERNS

Reynolds number (Re) is a dimensionless ratio of blood inertial forces to viscous forces. For a given vessel geometry, Re determines whether the flow was laminar or turbulent (Chatzizisis et al., 2007; Ku, 1997; Vlachopoulos, 2005). Re was calculated using $Re=(V*D*\rho)/\mu$, where V is peak blood flow velocity, D is artery diameter, ρ is blood density, and μ is blood viscosity (O'Rourke & Nichols, 2005). To determine the onset of turbulence under pulsatile flow conditions, it was calculated by peak Re critical using $Re_{peak}(cr)=169*\alpha^{0.83}*St^{-0.27}$, where St is the Strouhal number $St=freq*D*V$ and α is the Womersley parameter (Chatzizisis et al., 2007; Peacock et al., 1998).

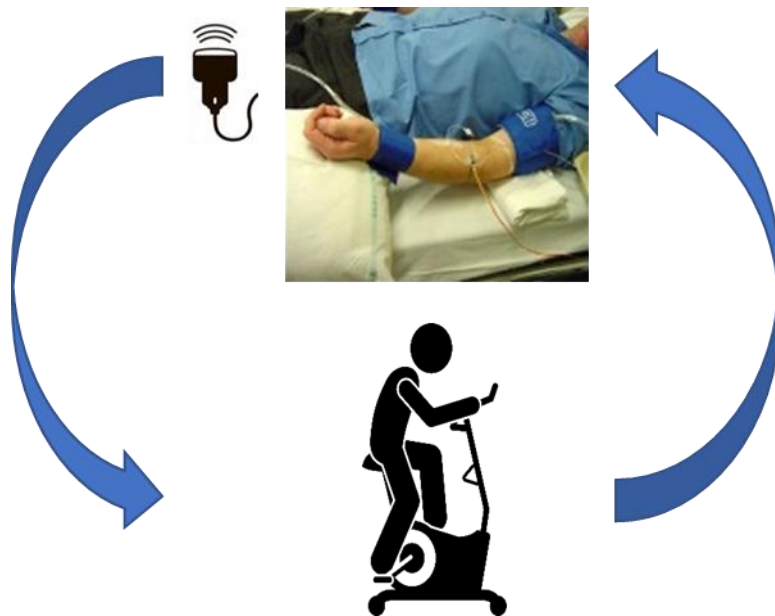


Figure 4 Visit 3

STATISTICAL ANALYSIS

Data was extracted from each instrument and compiled into a master data sheet in excel. Data was then then exported into RStudio to be analyzed with R statistical programming language. Data normality was assessed via visual analysis of a histogram and via quantitative means using the Shapiro-Wilk test. For hypothesis one, a series of two linear mixed effects models was conducted to determine differences in blood flow patterns and endothelial shear stress at low, moderate, and high exercise intensity; for the linear models, condition and sex was entered in the model as fixed factors while the participants were entered as random factors. Thereafter, a pair-wise post hoc test was conducted using a Holm-Bonferroni adjustment. Then, the magnitude of the difference was determined via a standardized difference using the Cohen's d effect size with Hedge's g correction for a small sample size. For hypothesis two, a series of paired t-tests or Wilcoxon signed rank-sum test for non-parametric data was utilized to determine the changes in FMD and VOP after eccentric exercise. When statistically significant, the magnitude of the differences was determined via Cohen's d with Hedges' correction for normally distributed variables and via the Wilcoxon effect size for non-normally distributed data. Statistical significance was set at an alpha level of 0.05.

Results

DESCRIPTIVES

Descriptive data are represented in mean, sd, and standard error of the mean in Table 1 for all of the participants and grouped by Sex (Female and Male).

Table 1. Descriptive Data

vars	mean	sd	se
Age (yrs)	22.10	2.91	0.69
Height (m)	1.60	0.08	0.02
Weight (kg)	67.60	17.81	4.20

VO2max (ml/kg)	32.40	5.52	1.30
HR	176.00	14.75	3.48
Lactate (mmol/L)	6.90	1.89	0.45
RPE	17.40	1.88	0.44
<i>Females</i>			
Height (m)	1.60	0.05	0.02
Weight (kg)	59.70	11.47	3.63
Age (yrs)	21.50	1.96	0.62
VO2max	31.70	5.91	1.87
HR	180.60	14.92	4.72
Lactate	6.90	1.67	0.53
RPE	17.80	1.87	0.59
<i>Males</i>			
Height	1.70	0.08	0.03
Weight	77.6 1	9.97	7.06
Age	22.90	3.80	1.34
VO2max	33.30	5.25	1.86
HR	170.2 1	3.19	4.66
Lactate	6.90	2.26	0.80
RPE	16.90	1.89	0.67

Table 2. Descriptive data are represented in mean, sd, and standard error of the mean for all the participants and grouped by Sex (Female and Male) during eccentric exercise on visit 2.

	Female				Male			
	Baseline (N=10)	Low (N=10)	Moderate (N=10)	High (N=10)	Baseline (N=8)	Low (N=8)	Moderate (N=8)	High (N=8)
HR								
Mean (SD)	75.0 (7.80)	114 (27.9)	134 (26.7)	160 (19.3)	84.1 (14.3)	110 (21.4)	125 (27.9)	154 (15.7)
RPE								
Mean (SD)	6.00 (0)	9.20 (1.87)	12.6 (2.01)	14.8 (2.78)	6.00 (0)	8.13 (2.17)	10.8 (2.66)	14.3 (3.11)
VO2								
Mean (SD)	5.25 (1.04)	15.5 (4.14)	19.4 (5.28)	23.7 (7.34)	5.34 (1.27)	15.0 (3.72)	22.5 (3.46)	28.6 (8.17)
Lactate								
Mean (SD)	0.84 (0.246)	1.50 (0.767)	2.23 (1.36)	2.83 (1.83)	0.963 (0.288)	1.71 (1.59)	3.45 (4.53)	3.28 (1.96)
Workload								
Mean (SD)	0(0)	51.5 (22.6)	87.5 (17.2)	120 (20.5)	0 (0)	56.3 (27.7)	106 (26.9)	155 (31.6)

DATA NORMALITY

Data was normally distributed for Re in all stages ($p > 0.05$), while it was also normally distributed in ESS for baseline, low, and high, but not moderate ($p = 0.03$). Hence, data for endothelial shear stress (ESS) and blood flow patterns (RE) were be treated as normally distributed. Flow mediated dilation was not normally distributed. For VOP, upper basal and lower body ischemia were normally distributed, while the rest of the variables were not normally distributed.

Endothelial Shear Stress and Blood Flow Patterns Results

There was an interaction of exercise intensity on antegrade ESS ($F(3,53.7)=26.90$, $p<0.001$), but not Sex ($p>0.05$), and a random effect of participant ($p < 0.001$). Post-hoc testing, all conditions to be significantly different from each other with a large effect, to the exception of low vs moderate ($p = 0.904$) (Table 2).

Table 3. Pairwise comparisons and Effect Size between exercise intensities on antegrade ESS.

group1	group2	statistic	p	Effect Size	magnitude
Baseline	Low	-4.99	0.00	-1.12	large
Baseline	Moderate	-4.40	0.00	-0.99	large
Baseline	High	-8.08	0.00	-1.87	large
Low	Moderate	-0.12	0.90	-0.03	negligible
Low	High	-5.13	0.00	-1.19	large
Moderate	High	-4.60	0.00	-1.06	large

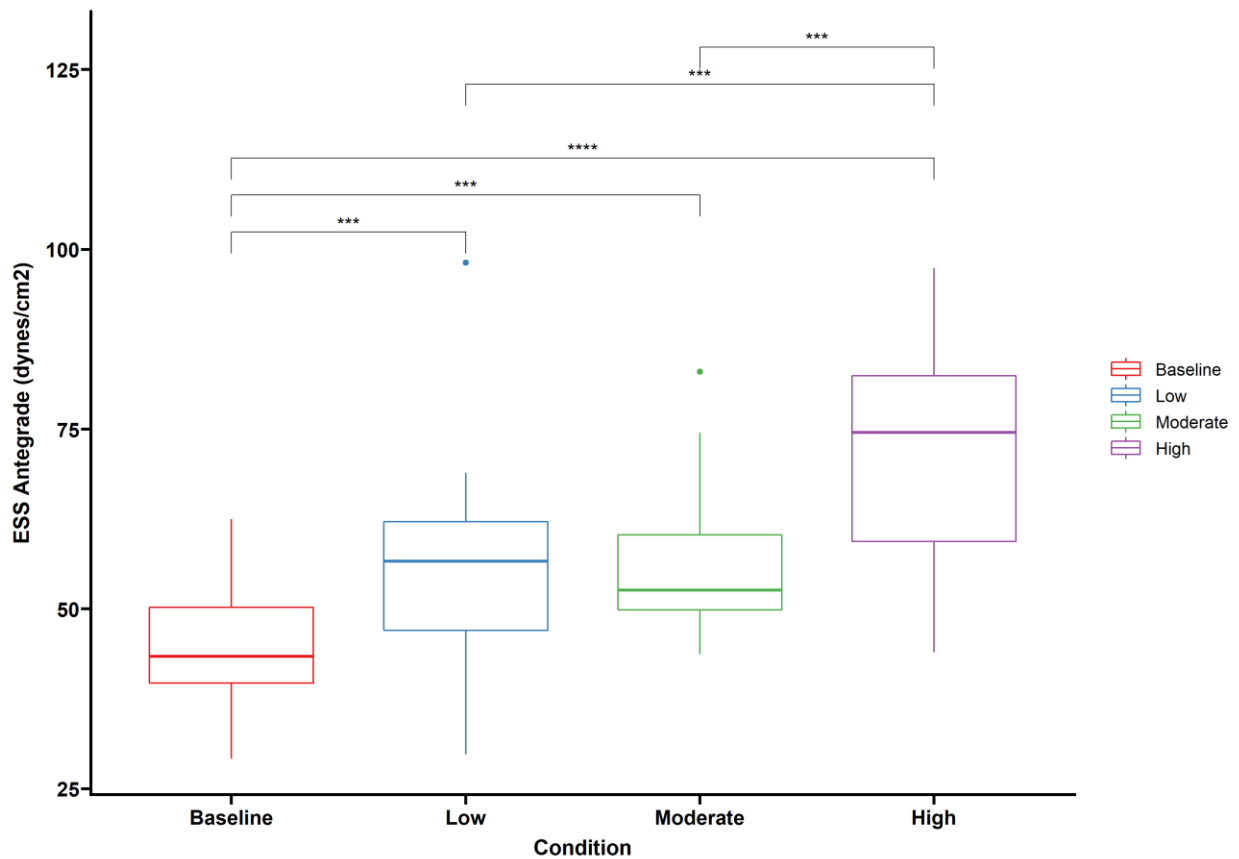


Figure 5. ESS antegrade for all intensities.

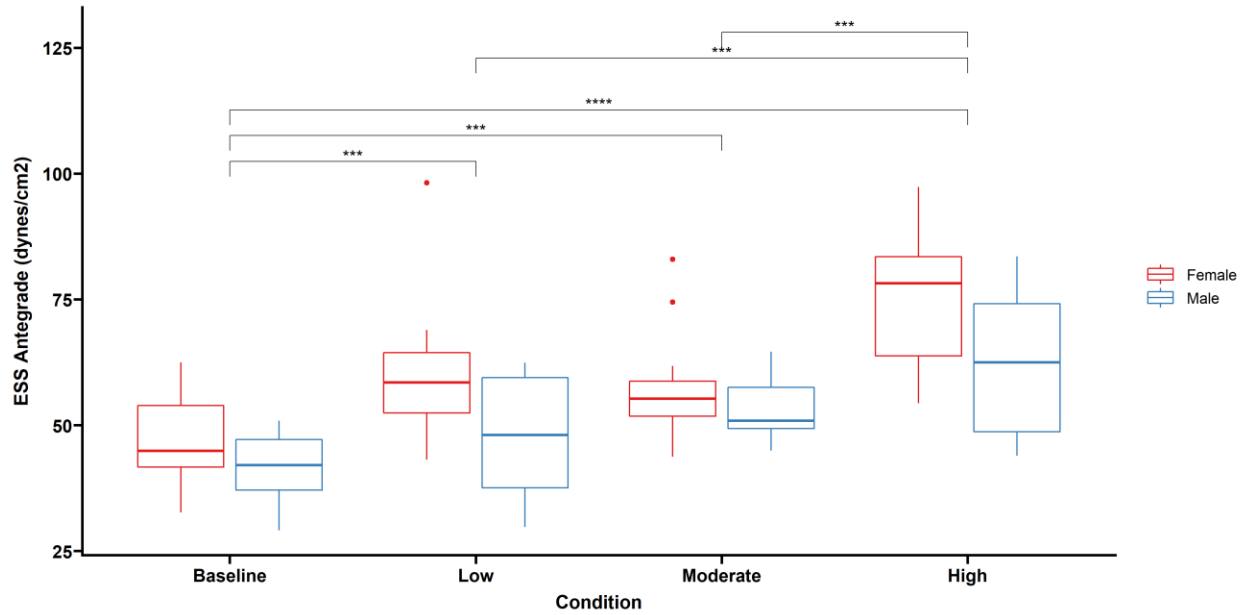


Figure 6. ESS Antegrade between intensities and sex.

There was an interaction of condition on retrograde ESS ($F(3,53.4)=11.21, p<0.001$), but not Sex ($p>0.05$), and a random effect of participant ($p < 0.001$). Post hoc pairwise comparisons showed a large effect difference between Baseline and Moderate, and Low and Moderate, and a moderate effect difference between Baseline and Low, and Low and High ($p<0.05$), with no difference between Low and High, and Moderate and High for ESS retrograde (Table 3).

Table 4. Pairwise comparisons and Effect Size between exercise intensities on ESS retrograde.

group1	group2	statistic	p.adj	effsize	magnitude
Baseline	Low	-3.20	0.02	-0.72	moderate
Baseline	Moderate	-8.00	0.00	-1.80	large
Baseline	High	-3.10	0.02	-0.72	moderate
Low	Moderate	-4.10	0.00	-0.92	large
Low	High	-2.00	0.13	-0.46	small
Moderate	High	0.20	0.85	0.05	negligible

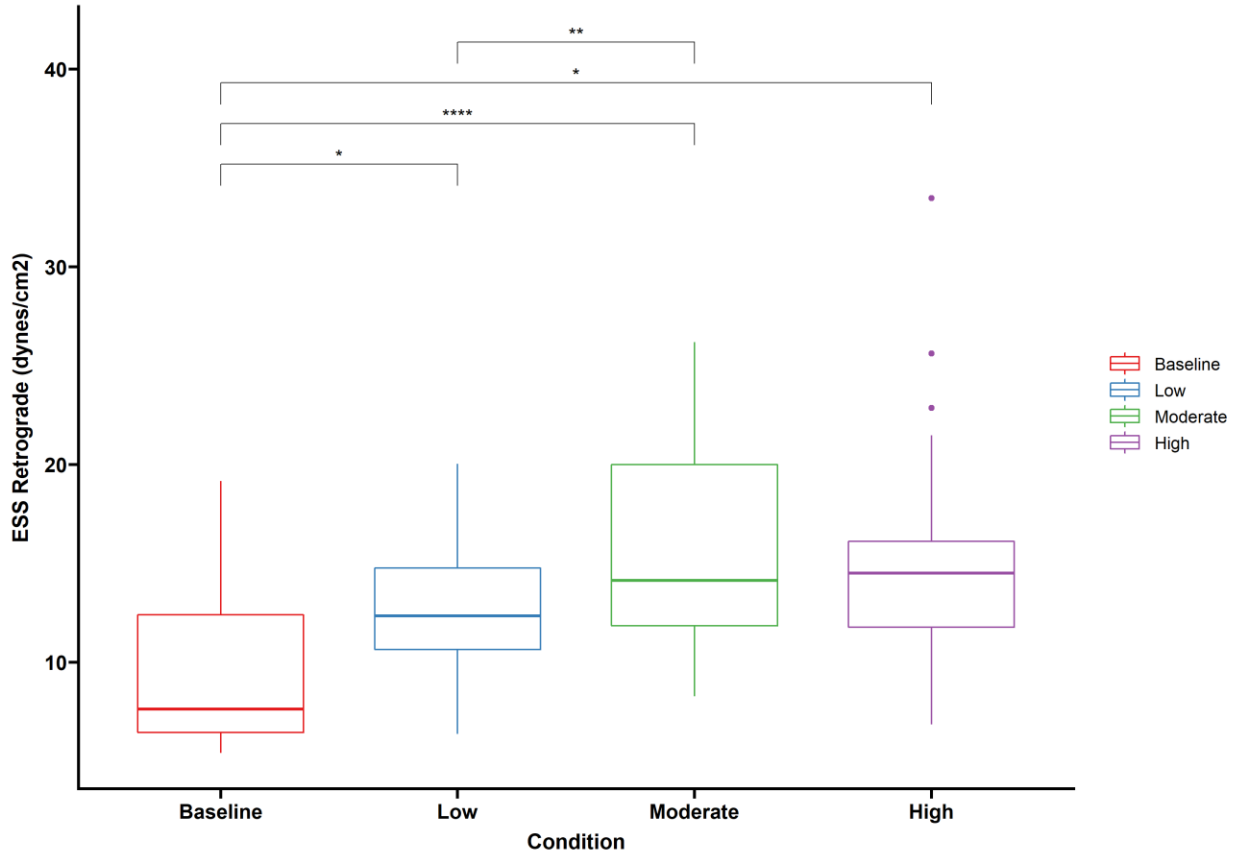


Figure 7. ESS retrograde for all intensities.

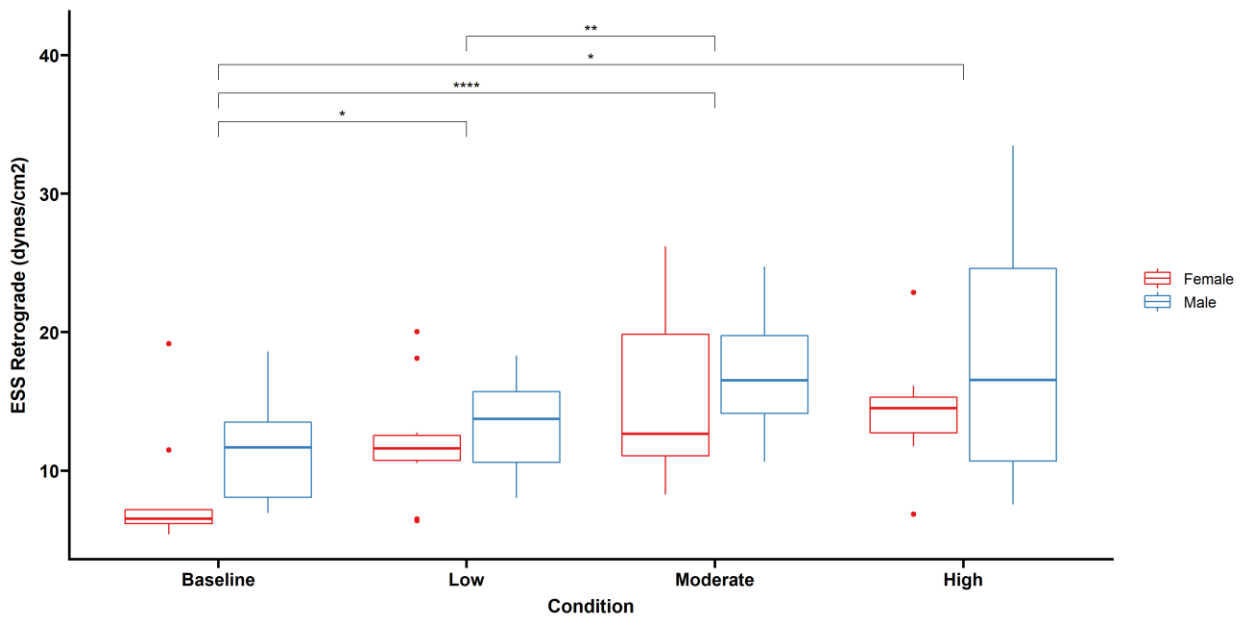


Figure 8. ESS retrograde between intensities and sex.

There was an interaction of condition on antegrade Re ($F(3,53.6)=25.03, p<0.001$), but not Sex or random effect of participant ($p>0.05$). Post hoc pairwise comparisons a large effect size for all comparisons ($p<0.05$) to the exception of low vs moderate ($p>0.05$) (Table 4).

Table 5. Pairwise comparisons and Effect Size between exercise intensities on antegrade RE.

group1	group2	statistic	p	effsize	magnitude
Baseline	Low	-4.20	0.00	-0.94	large
Baseline	Moderate	-4.70	0.00	-1.06	large
Baseline	High	-7.20	0.00	-1.67	large
Low	Moderate	-1.00	0.31	-0.24	small
Low	High	-5.70	0.00	-1.32	large
Moderate	High	-4.80	0.00	-1.12	large

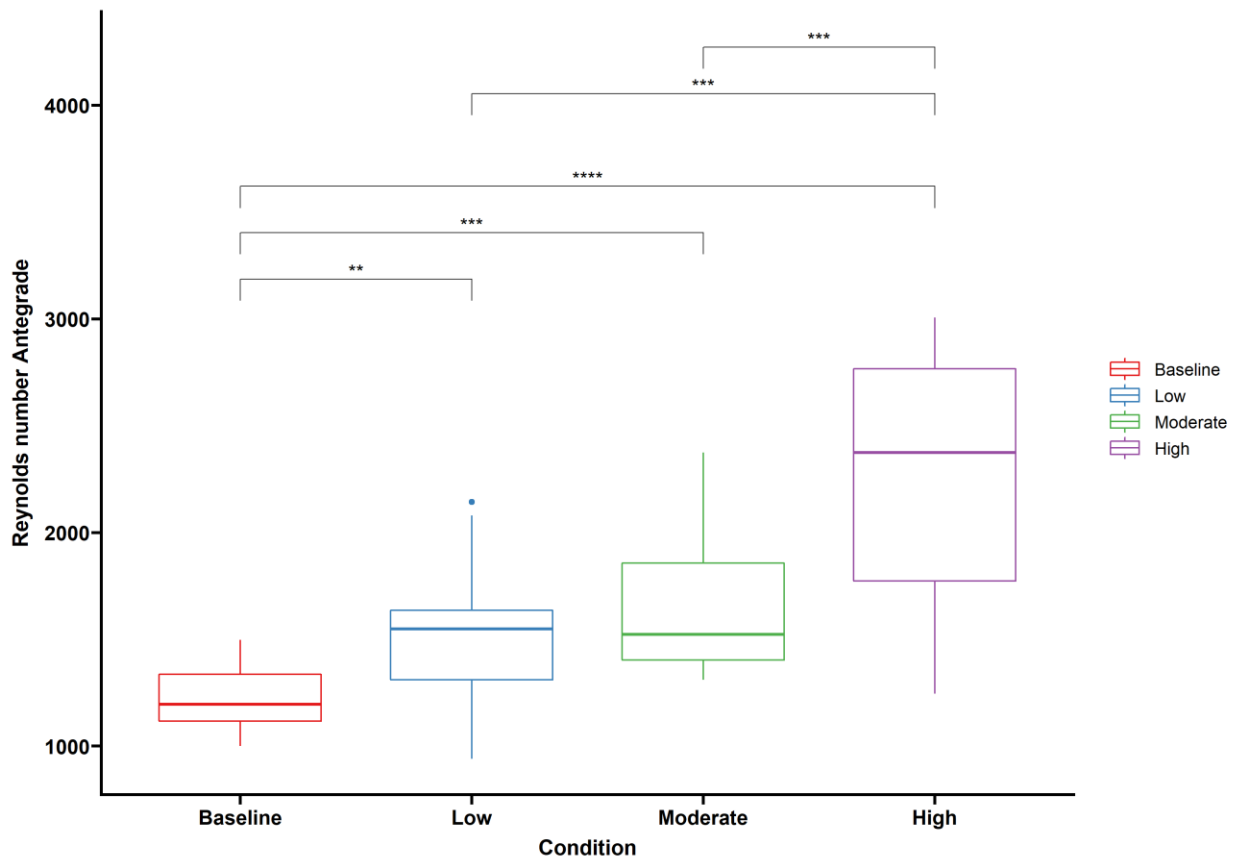


Figure 9. Reynolds number antegrade by intensity.

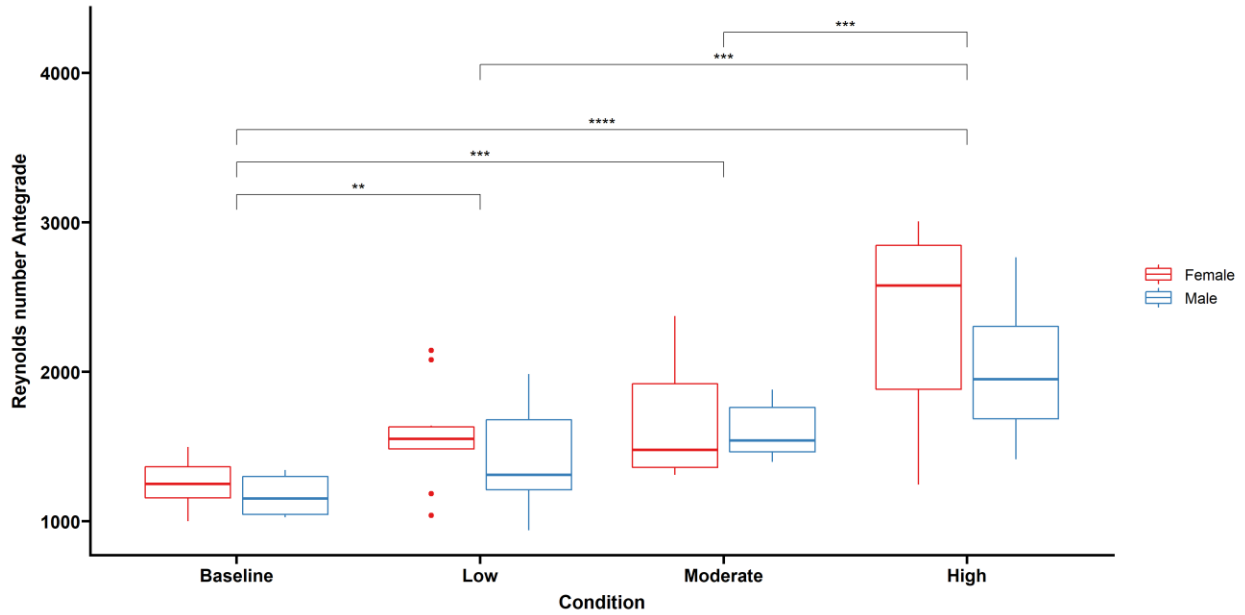


Figure 10. Reynolds number antegrade by intensity and sex.

There was an interaction of condition on retrograde Re ($F(3,54.3)=12.34, p<0.001$), Sex ($F(1,18.5)=4.41, p=0.05$), and random effect of participant ($p>0.05$). Post hoc pairwise comparisons a large effect size for all comparisons ($p<0.05$) to the exception of low vs moderate ($p>0.05$) (Table 5).

Table 6. Pairwise comparisons and Effect Size between exercise intensities on retrograde RE.

group1	group2	statistic	p.adj	Effect size	magnitude
Baseline	Low	-3.20	0.02	-0.72	moderate
Baseline	Moderate	-6.69	0.00	-1.51	large
Baseline	High	-3.34	0.02	-0.77	moderate
Low	Moderate	-6.62	0.00	-1.49	large
Low	High	-2.58	0.04	-0.60	moderate
Moderate	High	-0.38	0.71	-0.09	negligible

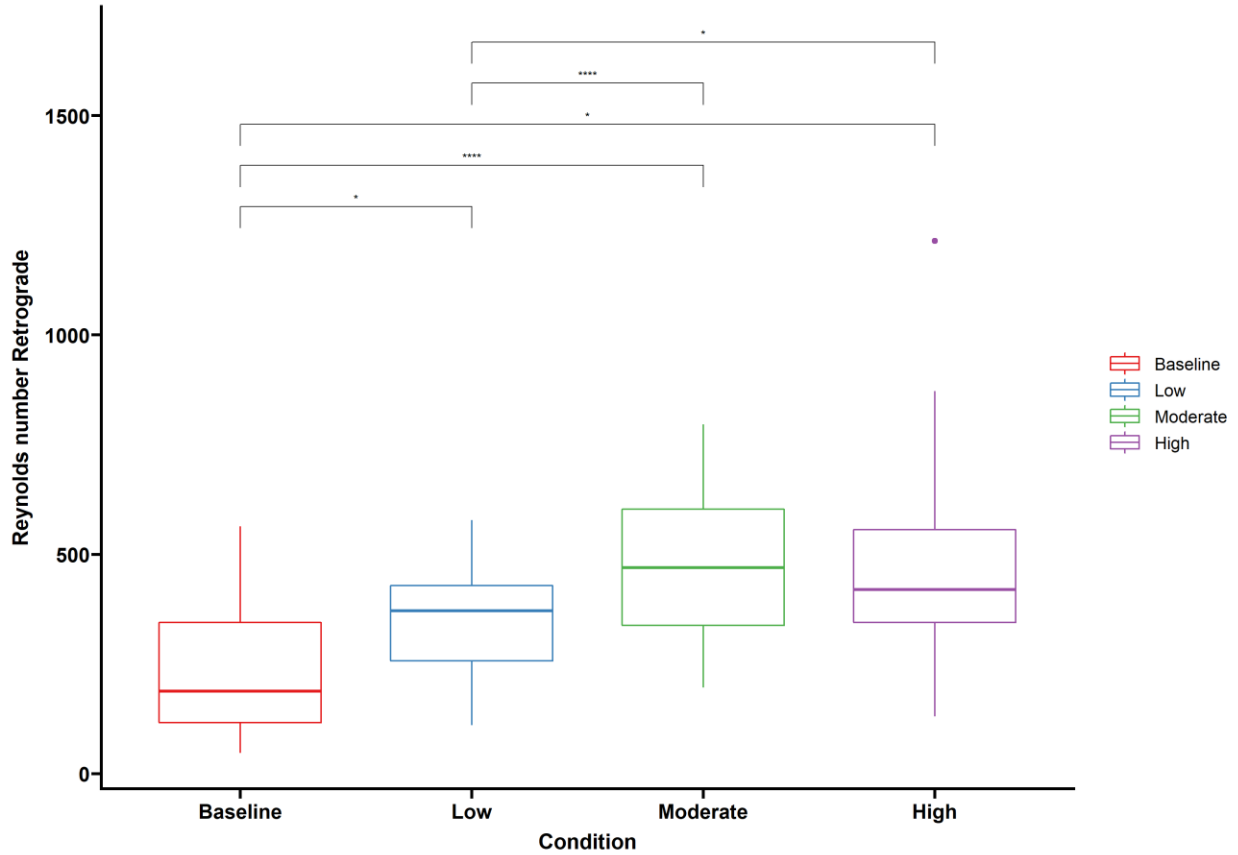


Figure 11. Reynolds number retrograde by intensity.

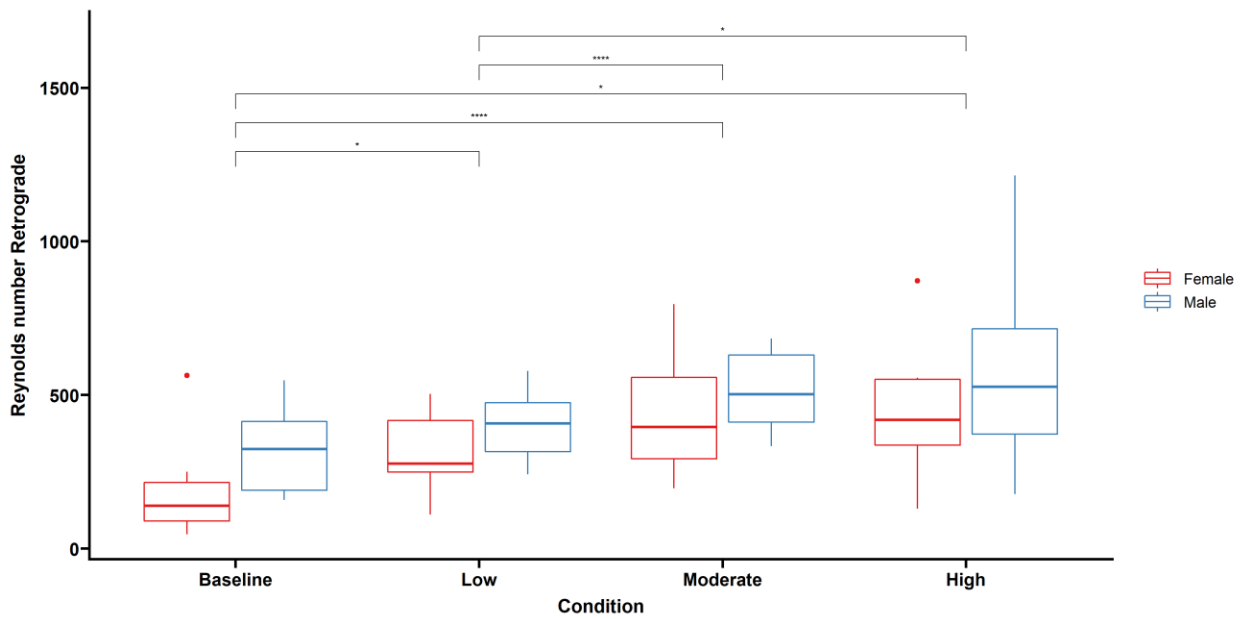


Figure 12. Reynolds number retrograde by intensity and sex,

Flow Mediated Dilation and Venous Occlusion Plethysmography Results

There was no difference from pre to post on FMD ($p > 0.05$). For VOP variables, there were significant changes with a moderate effect size in Upper Basal, Upper Ischemia ($p < 0.05$), And no changes in Upper post ischemia, lower basal, lower ischemia, or lower post ischemia ($p > 0.05$) (Table 6). In addition, there were no differences in FMD basal diameter, FMD peak diameter, or FMD % difference between basal and peak from pre to post ($p < 0.05$).

Table 7. T test or Wilcoxon test for pre to post differences with Hedge’s g or Wilcoxon’s effect size.

	t or w	p	effect size*	magnitude
FMD	185.00	0.30	0.18	small
Upper Basal	2.41	0.03	0.65	moderate
Upper Ischemia	132.00	0.02	0.47	moderate
Upper Post ischemia	78.00	0.80	0.07	small
Lower Basal	92.00	1.00	0.01	small
Lower Ischemia	0.72	0.48	0.41	small
Lower Post ischemia	69.00	0.80	0.05	small

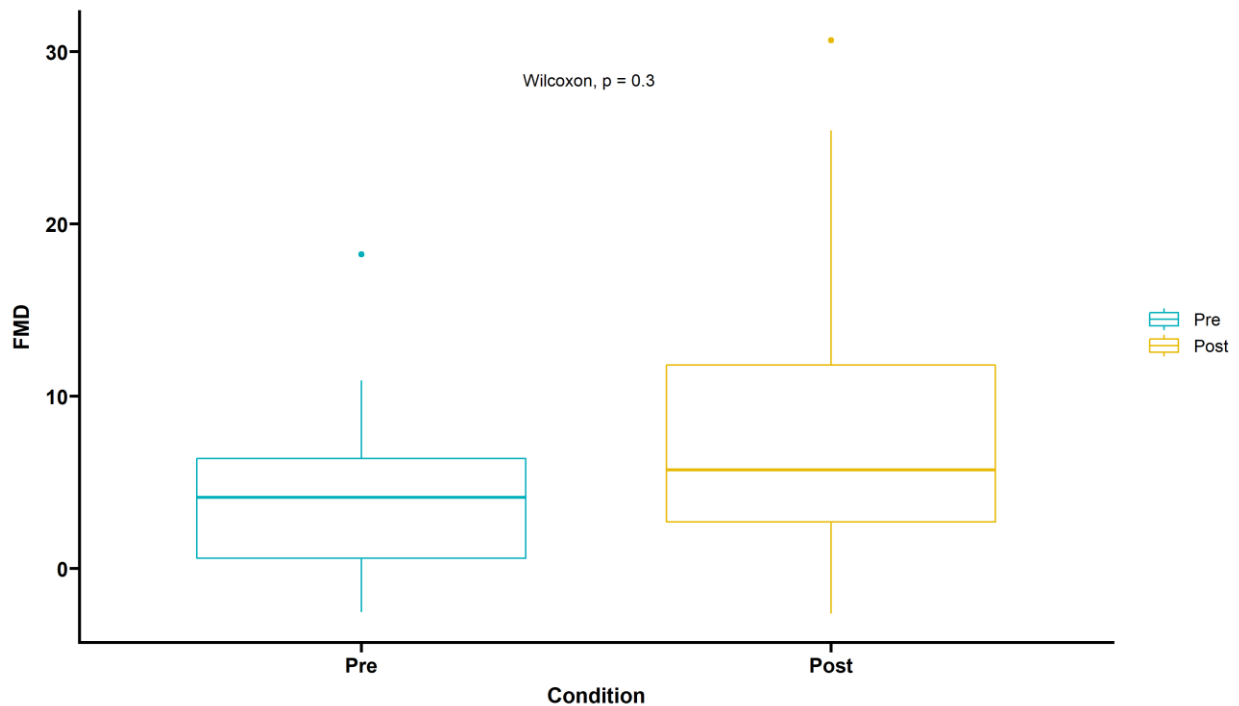


Figure 13. FMD pre to post

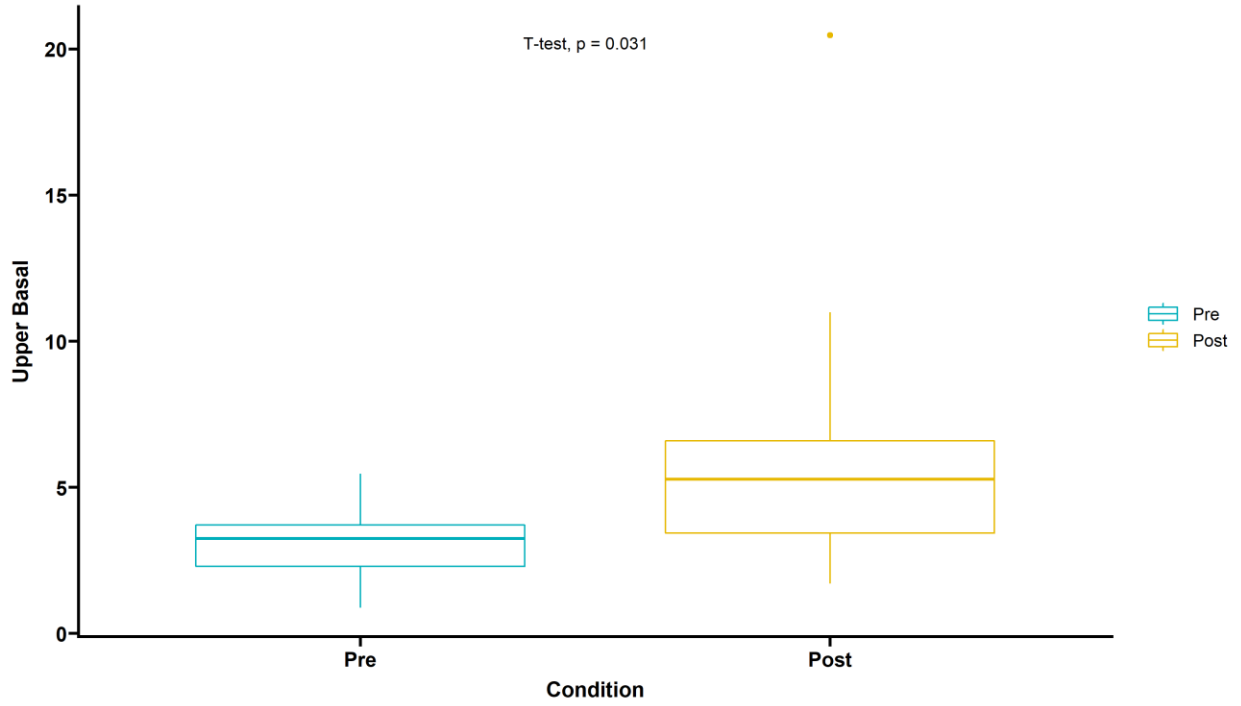


Figure 14. Upper basal.

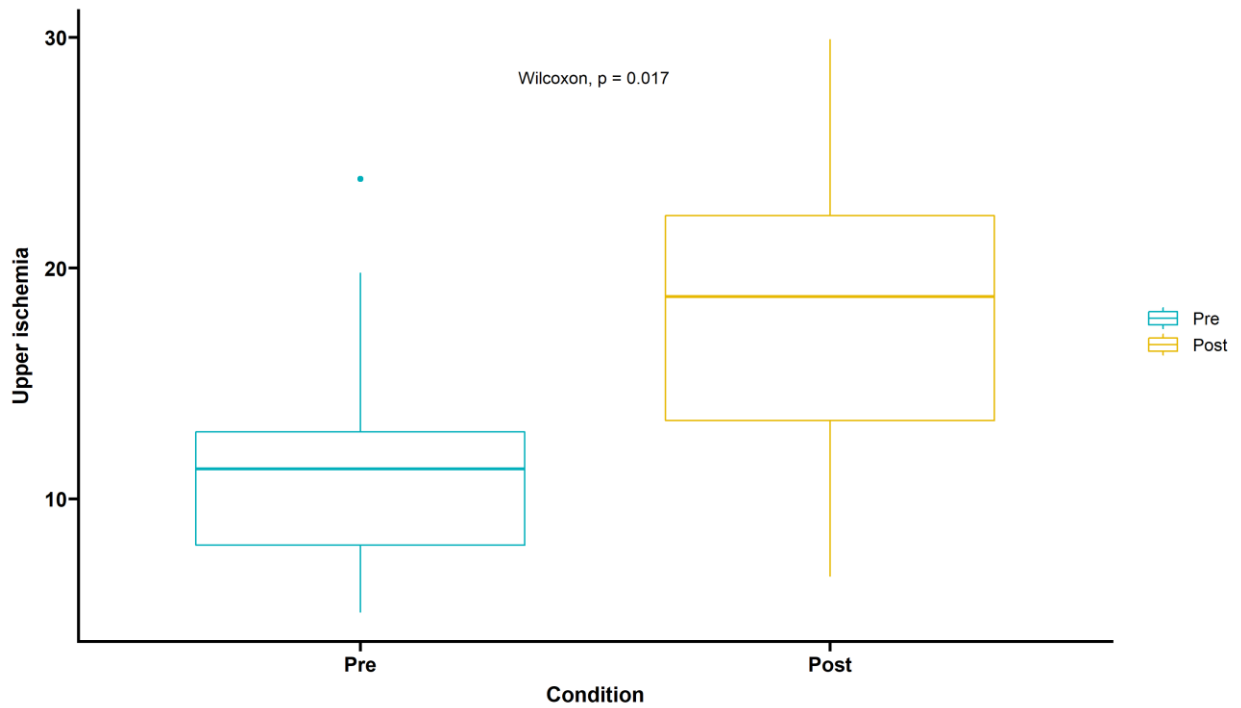


Figure 15. Upper ischemia.

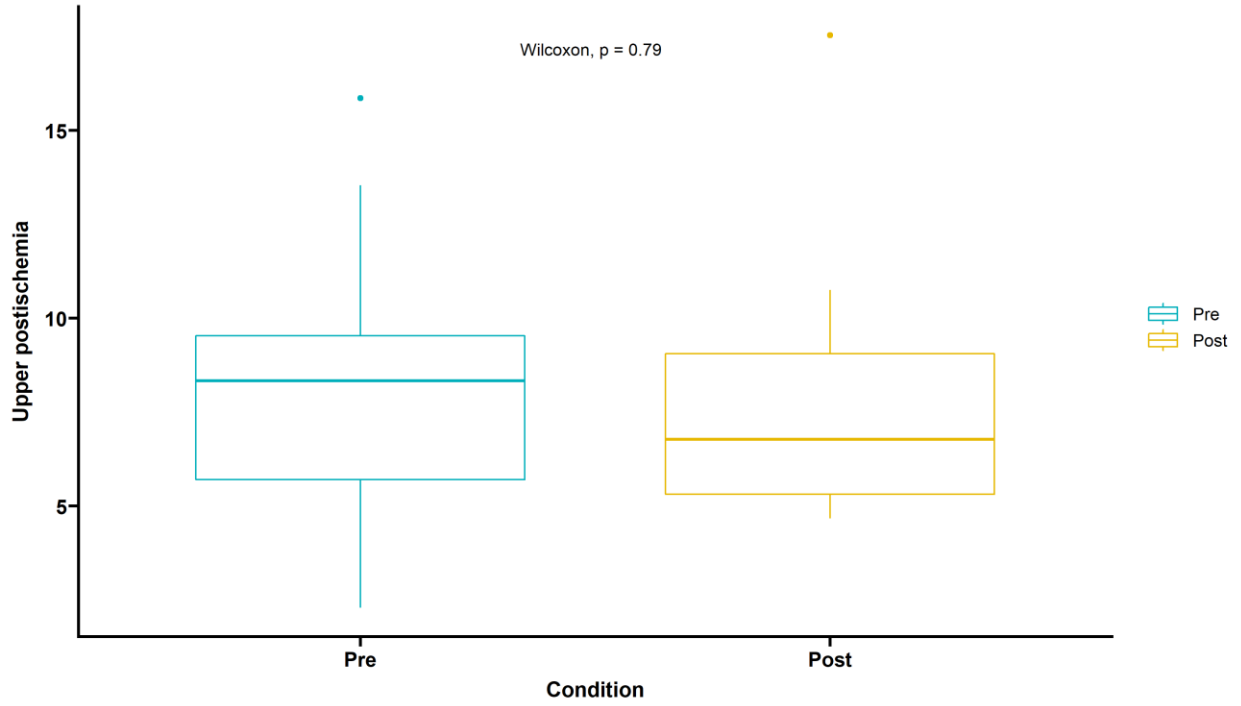


Figure 16. Upper postischemia.

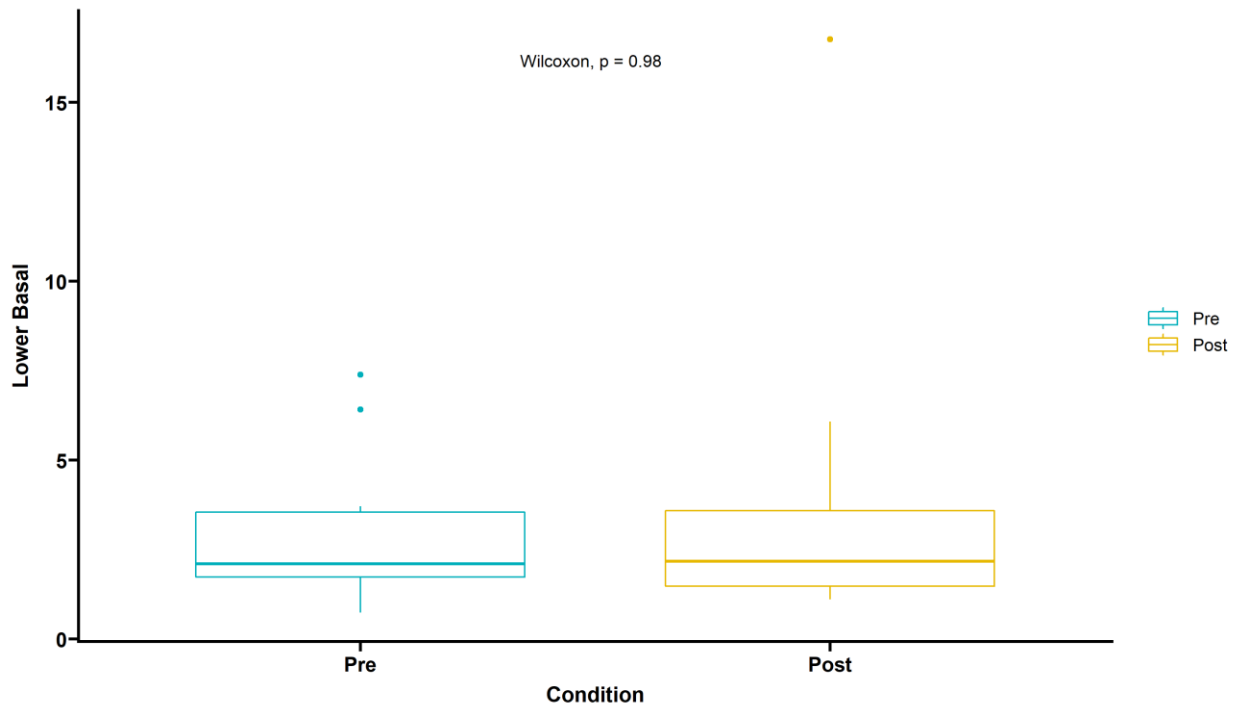


Figure 17. Lower basal.

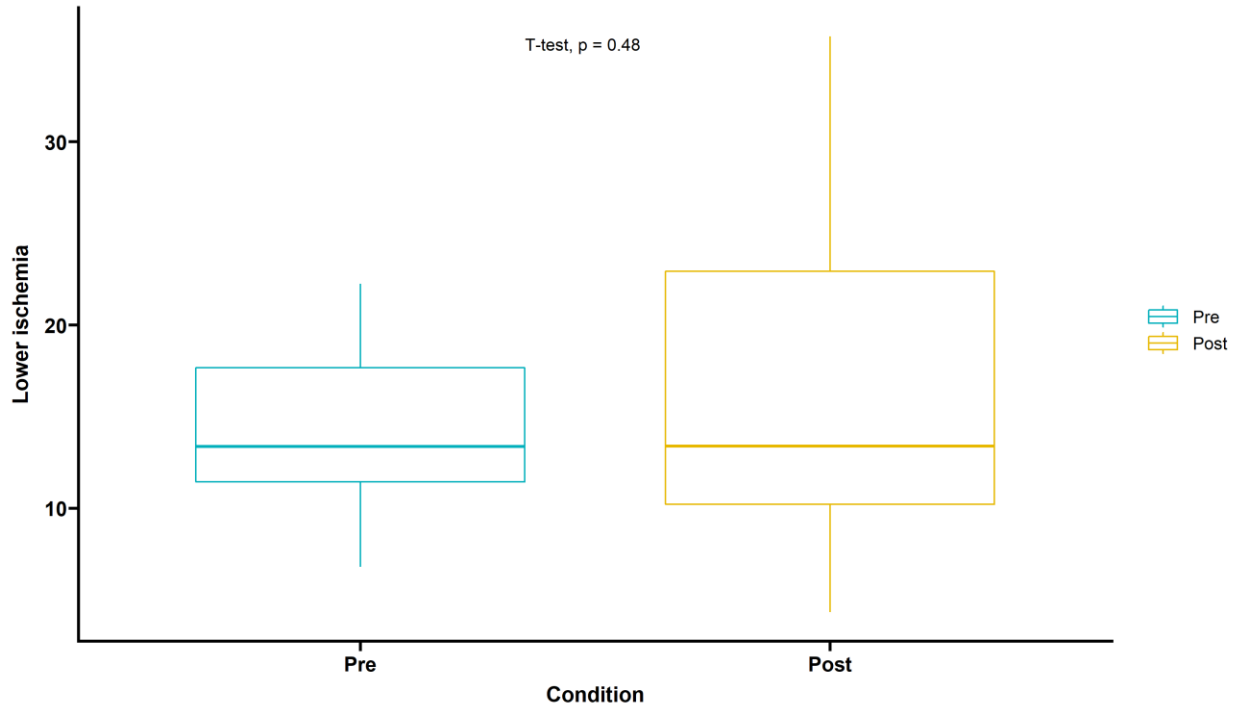


Figure 18. Lower ischemia.

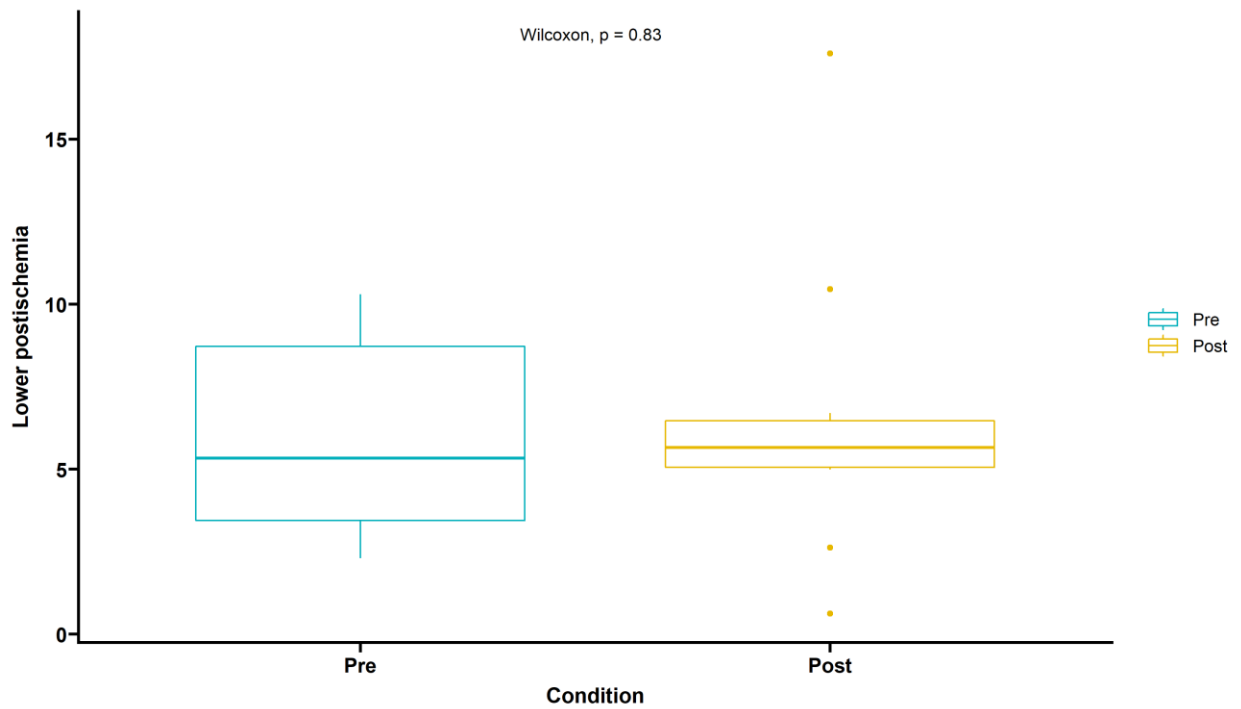


Figure 19. Lower extremity postischemia.

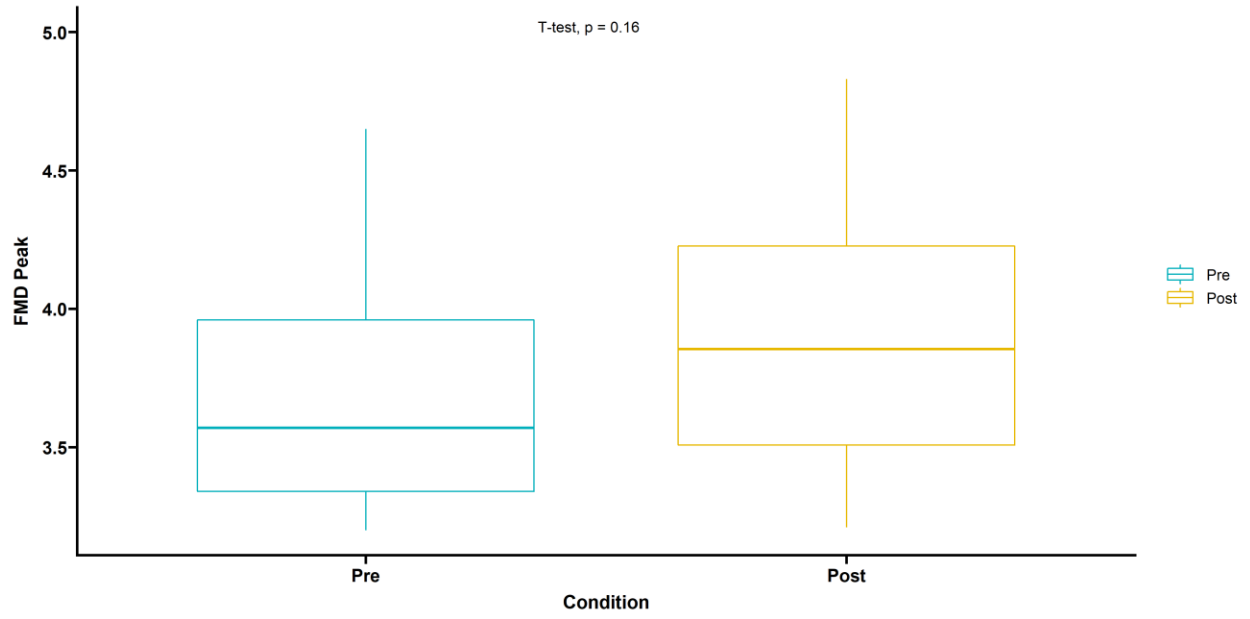


Figure 20. FMD pre and post peak.

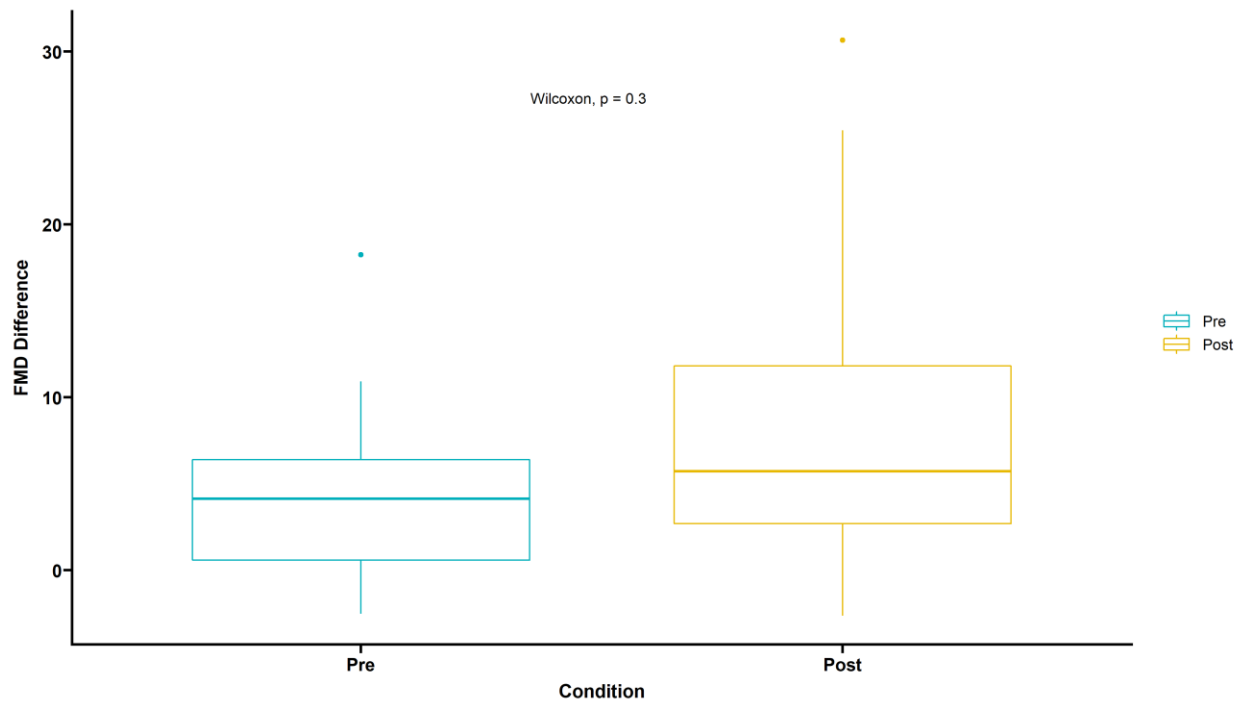


Figure 21. FMD pre and post difference.

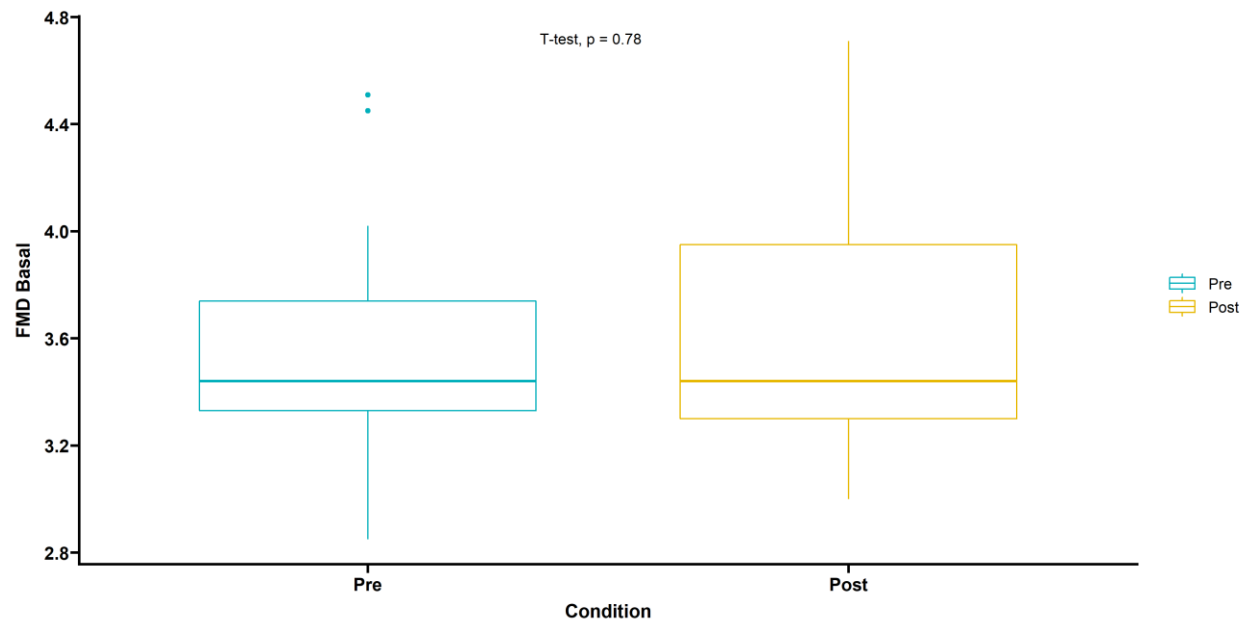


Figure 22. FMD pre and post basal measurement.

Table 8. FMD pre and post, baseline, peak and difference.

Variable	Pre			Post		
	Mean	SD	SE	Mean	SD	SE
Baseline	3.55	0.47	0.11	3.61	0.47	0.11
Peak	3.71	0.42	0.10	3.93	0.45	0.11
FMD difference	4.81	5.46	1.32	9.31	0.45	2.17

Discussion

The present study is the first study, to the best of our knowledge, to investigate the blood flow patterns and vascular reactivity during eccentric cycling exercise. The major findings in this study are twofold. First, and as observed during concentric cycling, eccentric cycling produces exercise-induced blood flow patterns (i.e., ESS and turbulent flow) that are intensity dependent. Secondly, eccentric cycling enhanced blood flow in the upper but not in the lower extremities, which could be associated with increased endothelial function.

Hence the primary findings showed a significant effect of exercise intensity on ESS and turbulent flow, both antegrade and retrograde, confirming that ECC produces exercise-induced blood flow patterns changes in the brachial artery. There is no previous study, to the best of our knowledge, investigating blood flow patterns during eccentric cycling. The results of the present study are similar to our previous work (Alvaro N. Gurovich et al., 2021; A. N. Gurovich et al., 2021) evaluating blood flow patterns through intensities on a concentric cycling ergometer. During concentric cycling, ESS ranged ~ 50 to ~ 80 dynes/cm² in antegrade ESS and ~ 20 to ~ 30 dynes/cm² in retrograde ESS. The current study observed ESS levels of ~ 50 - 75 and ~ 15 - 18 dynes/cm² in antegrade and retrograde ESS, respectively, confirming these similar findings. (A. N. Gurovich et al., 2021). Regarding turbulent flow the present study showed that blood flow is primary turbulent only at medium and high intensities in antegrade flow (Figures 5 and 7). In contrast, and interestingly, our previous studies have shown turbulent flow at all exercise intensities, both at antegrade and retrograde flow (Gurovich 2021). This difference could be attributed that the present study did not normalize Re by the Womersley factor, underestimating turbulence. Therefore, we could assume similar results when comparing ECC and concentric cycling. (A. N. Gurovich et al., 2021). Finally, and as previously reported in concentric cycling,

ECC cycling produces exercise intensity-dependent, bi-directional, and turbulent blood flow in the brachial artery (A. N. Gurovich et al., 2021) (Coovert et al., 2018; Gurovich & Braith, 2013).

The current study is the first to evaluate the effects of a bout of eccentric cycling on peripheral blood flow. Interestingly, the results of the present study showed that blood flow increases in the upper extremity but did not change in the lower extremities, where most of the work is performed. Brachial artery diameter (table 6) and forearm VOP (figure 11) increased after one bout of ECC exercise. This increase could be associated with the increase in ESS and NO bioavailability previously presented. However, VOP in the calf (figure 18) did not increase after exercise. This lack of increased blood flow to the lower extremities could be associated to 2 factors: 1) the lower metabolic demands that ECC produced and 2) a local decrease in sympatholysis. ECC is lower metabolically demanding according to Peñailillo, smaller demands have been noted in oxygen consumption and heart rate (Peñailillo et al., 2013). Oxygen consumption during ECC was approximately 50% of that during CON for the same workload, which confirms ECC metabolic demands are lower than CON (Knuttgen et al., 1982; Peñailillo et al., 2013; Perrey et al., 2001). During exercise, skeletal muscle blood flow is regulated depending on metabolic mechanisms. Therefore due to the lower metabolic demands of ECC, the decrease of blood flow towards is noted with the smaller metabolic demand of oxygen consumption throughout ECC.

On the other hand, sympatholysis is defined as the a protective mechanism to optimize muscle blood flow distribution to match perfusion with metabolic demand (Thomas, 2015). There is a good agreement that functional sympatholysis is not an all-or – none phenomenon, but rather a continuum of vascular responsiveness that varies inversely with the strength of vasoconstrictor stimulus and directly with the intensity of the muscular work (Thomas, 2015; Thomas & Segal,

2004). Within skeletal muscle microcirculation, functional sympatholysis is more pronounced in the small distal arterioles than in the large proximal arterioles and feed arteries (Thomas, 2015) Which allows the most metabolically active muscle fibers, to be optimally perfused by the dilated distal vessels while retaining the ability constrict the proximal vessels and regulate systemic arterial pressure (Anderson & Faber, 1991; Boegehold & Johnson, 1988; Folkow et al., 1971; Thomas, 2015; VanTeeffelen & Segal, 2003). In this case, ECC would increase sympathetic drive to the muscles of the legs without an increased in metabolic demands what will maintain blood flow steady after ECC exercise in the lower extremities.

In general, endothelial function does not increase after a bout of acute exercise. The results of the present study are in agreement with previous studies in traditional/concentric cycling (Caldwell et al., 2016; Haynes et al., 2017; Rakobowchuk et al., 2017; Stacy, 2011; Stacy et al., 2013)). Endothelial function measurement via FMD with an exposure to eccentric cycling has been vaguely studied, with only a few studies investigating this matter (Caldwell et al., 2016; Haynes et al., 2017; Rakobowchuk et al., 2017; Stacy, 2011; Stacy et al., 2013). Our results showed no changes in FMD post exercise when compared to before exercise. Similar results were observed by Haynes et al., Rakobowchuk et al., Stacy et al., and Stacy et al.; however, all report an increment of brachial artery diameter post exercise (Haynes et al., 2017; Rakobowchuk et al., 2017; Stacy, 2011; Stacy et al., 2013), which was also observed in the current study. Even though an evident increment in baseline diameters in all previous studies including current study in pre-condition, the increment of post diameter should be consider that both variables of FMD% change increase. In the current study all diameters increment baseline diameter increase by 1% where post-deflation an increase of 5% was shown. Therefore not only should the lack of significance should be implied to the increment of baseline diameter on both

pre/post conditions but to an overall scope of physiological changes that occur in a cascade of events that primordial changes occur in the microcirculation then to macrocirculation. It is expected that chronic exposure to ECC could improve endothelial function after training; however, those studies have not been performed.

LIMITATIONS

The present study is not exempt from limitations. Our study was limited to the sample size. Our between-subjects comparison analyzes could have been compromised by the low sample size. As well as the absence of a direct comparison of concentric versus eccentric assessment. In addition, we did not perform FMD in the lower extremity (e.g. popliteal FMD), which could have helped confirming some of the results observed with VOP.

CONCLUSION

In conclusion, eccentric cycling exercise produces exercise-induced blood flow patterns that are intensity dependent, similar to traditional/concentric cycling. A single bout of ECC cycling produces an increase in blood flow in the upper extremity, associated with increased ESS, but not in the lower extremity. The lack of increased blood flow in the lower extremities could be associated with lower metabolic demands and decreased functional sympatholysis. Blood flow patterns throughout different intensities providing that eccentric exercise could be beneficiary for specific populations that suffer CVD, COPD, stroke, and those who fail to maintain a high metabolic demand through an exercise bout.

References

- Abbott, B. C., Bigland, B., & Ritchie, J. M. (1952, Jul). The physiological cost of negative work. *J Physiol*, 117(3), 380-390. <https://doi.org/10.1113/jphysiol.1952.sp004755>
- Abramson, J. L., & Vaccarino, V. (2002, Jun 10). Relationship between physical activity and inflammation among apparently healthy middle-aged and older US adults. *Arch Intern Med*, 162(11), 1286-1292. <https://doi.org/10.1001/archinte.162.11.1286>
- Adkisson, E. J., Casey, D. P., Beck, D. T., Gurovich, A. N., Martin, J. S., & Braith, R. W. (2010, Jan). Central, peripheral and resistance arterial reactivity: fluctuates during the phases of the menstrual cycle. *Exp Biol Med (Maywood)*, 235(1), 111-118. <https://doi.org/10.1258/ebm.2009.009186>
- Allen, J. D., Cobb, F. R., Kraus, W. E., & Gow, A. J. (2006, Sep 1). Total nitrogen oxide following exercise testing reflects endothelial function and discriminates health status. *Free Radic Biol Med*, 41(5), 740-747. <https://doi.org/10.1016/j.freeradbiomed.2006.05.016>
- Anderson, K. M., & Faber, J. E. (1991, Jul). Differential sensitivity of arteriolar alpha 1- and alpha 2-adrenoceptor constriction to metabolic inhibition during rat skeletal muscle contraction. *Circ Res*, 69(1), 174-184. <https://doi.org/10.1161/01.res.69.1.174>
- Atkinson, G., Batterham, A. M., Thijssen, D. H., & Green, D. J. (2013, Feb). A new approach to improve the specificity of flow-mediated dilation for indicating endothelial function in cardiovascular research. *J Hypertens*, 31(2), 287-291. <https://doi.org/10.1097/HJH.0b013e32835b8164>
- Boegehold, M. A., & Johnson, P. C. (1988, May). Response of arteriolar network of skeletal muscle to sympathetic nerve stimulation. *Am J Physiol*, 254(5 Pt 2), H919-928. <https://doi.org/10.1152/ajpheart.1988.254.5.H919>
- Caldwell, J. T., Wardlow, G. C., Branch, P. A., Ramos, M., Black, C. D., & Ade, C. J. (2016, Nov). Effect of exercise-induced muscle damage on vascular function and skeletal muscle microvascular deoxygenation. *Physiol Rep*, 4(22). <https://doi.org/10.14814/phy2.13032>
- Chatzizisis, Y. S., Coskun, A. U., Jonas, M., Edelman, E. R., Feldman, C. L., & Stone, P. H. (2007, Jun 26). Role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodeling: molecular, cellular, and vascular behavior. *J Am Coll Cardiol*, 49(25), 2379-2393. <https://doi.org/10.1016/j.jacc.2007.02.059>
- Chen, T. C., Chen, H. L., Lin, M. J., Wu, C. J., & Nosaka, K. (2010, May). Potent protective effect conferred by four bouts of low-intensity eccentric exercise. *Med Sci Sports Exerc*, 42(5), 1004-1012. <https://doi.org/10.1249/MSS.0b013e3181c0a818>

- Chen, T. C., Nosaka, K., & Wu, C. C. (2008, Jun). Effects of a 30-min running performed daily after downhill running on recovery of muscle function and running economy. *J Sci Med Sport*, *11*(3), 271-279. <https://doi.org/10.1016/j.jsams.2007.02.015>
- Coovert, D., Evans, L. D., Jarrett, S., Lima, C., Lima, N., & Gurovich, A. N. (2018, Oct). Blood flow patterns during incremental and steady-state aerobic exercise. *J Sports Med Phys Fitness*, *58*(10), 1537-1543. <https://doi.org/10.23736/s0022-4707.17.07142-0>
- Corretti, M. C., Anderson, T. J., Benjamin, E. J., Celermajer, D., Charbonneau, F., Creager, M. A., Deanfield, J., Drexler, H., Gerhard-Herman, M., Herrington, D., Vallance, P., Vita, J., & Vogel, R. (2002, Jan 16). Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. *J Am Coll Cardiol*, *39*(2), 257-265. [https://doi.org/10.1016/s0735-1097\(01\)01746-6](https://doi.org/10.1016/s0735-1097(01)01746-6)
- DeSouza, C. A., Shapiro, L. F., Clevenger, C. M., Dinunno, F. A., Monahan, K. D., Tanaka, H., & Seals, D. R. (2000, Sep 19). Regular aerobic exercise prevents and restores age-related declines in endothelium-dependent vasodilation in healthy men. *Circulation*, *102*(12), 1351-1357. <https://doi.org/10.1161/01.cir.102.12.1351>
- Ekelund, U., Ward, H. A., Norat, T., Luan, J., May, A. M., Weiderpass, E., Sharp, S. J., Overvad, K., Østergaard, J. N., Tjønneland, A., Johnsen, N. F., Mesrine, S., Fournier, A., Fagherazzi, G., Trichopoulou, A., Lagiou, P., Trichopoulos, D., Li, K., Kaaks, R., Ferrari, P., Licaj, I., Jenab, M., Bergmann, M., Boeing, H., Palli, D., Sieri, S., Panico, S., Tumino, R., Vineis, P., Peeters, P. H., Monnikhof, E., Bueno-de-Mesquita, H. B., Quirós, J. R., Agudo, A., Sánchez, M. J., Huerta, J. M., Ardanaz, E., Arriola, L., Hedblad, B., Wirfält, E., Sund, M., Johansson, M., Key, T. J., Travis, R. C., Khaw, K. T., Brage, S., Wareham, N. J., & Riboli, E. (2015, Mar). Physical activity and all-cause mortality across levels of overall and abdominal adiposity in European men and women: the European Prospective Investigation into Cancer and Nutrition Study (EPIC). *Am J Clin Nutr*, *101*(3), 613-621. <https://doi.org/10.3945/ajcn.114.100065>
- Fiuza-Luces, C., Santos-Lozano, A., Joyner, M., Carrera-Bastos, P., Picazo, O., Zugaza, J. L., Izquierdo, M., Ruilope, L. M., & Lucia, A. (2018, Dec). Exercise benefits in cardiovascular disease: beyond attenuation of traditional risk factors. *Nat Rev Cardiol*, *15*(12), 731-743. <https://doi.org/10.1038/s41569-018-0065-1>
- Flammer, A. J., Anderson, T., Celermajer, D. S., Creager, M. A., Deanfield, J., Ganz, P., Hamburg, N. M., Lüscher, T. F., Shechter, M., Taddei, S., Vita, J. A., & Lerman, A. (2012, Aug 7). The assessment of endothelial function: from research into clinical practice. *Circulation*, *126*(6), 753-767. <https://doi.org/10.1161/circulationaha.112.093245>
- Folkow, B., Sonnenschein, R. R., & Wright, D. L. (1971, Apr). Loci of neurogenic and metabolic effects on precapillary vessels of skeletal muscle. *Acta Physiol Scand*, *81*(4), 459-471. <https://doi.org/10.1111/j.1748-1716.1971.tb04924.x>

- Ghisi, G. L., Durieux, A., Pinho, R., & Benetti, M. (2010, Oct). Physical exercise and endothelial dysfunction. *Arq Bras Cardiol*, 95(5), e130-137. <https://doi.org/10.1590/s0066-782x2010001500025>
- González-Bartholin, R., Mackay, K., Valladares, D., Zbinden-Foncea, H., Nosaka, K., & Peñailillo, L. (2019, Oct). Changes in oxidative stress, inflammation and muscle damage markers following eccentric versus concentric cycling in older adults. *Eur J Appl Physiol*, 119(10), 2301-2312. <https://doi.org/10.1007/s00421-019-04213-7>
- Goto, C., Higashi, Y., Kimura, M., Noma, K., Hara, K., Nakagawa, K., Kawamura, M., Chayama, K., Yoshizumi, M., & Nara, I. (2003). Effect of Different Intensities of Exercise on Endothelium-Dependent Vasodilation in Humans. *Circulation*, 108(5), 530-535. <https://doi.org/doi:10.1161/01.CIR.0000080893.55729.28>
- Green, D. J., Hopman, M. T., Padilla, J., Laughlin, M. H., & Thijssen, D. H. (2017, Apr). Vascular Adaptation to Exercise in Humans: Role of Hemodynamic Stimuli. *Physiol Rev*, 97(2), 495-528. <https://doi.org/10.1152/physrev.00014.2016>
- Gurovich, A. N., & Braith, R. W. (2013, Apr). Enhanced external counterpulsation creates acute blood flow patterns responsible for improved flow-mediated dilation in humans. *Hypertens Res*, 36(4), 297-305. <https://doi.org/10.1038/hr.2012.169>
- Gurovich, A. N., Rodriguez, L., Gomez, M., Caraveo, P., Ochoa, L., & Morales-Acuna, F. (2021). Imaging Ultrasound Assessment of Exercise-Induced Endothelial Shear Stress of the Brachial and Carotid Arteries. *Cardiopulmonary Physical Therapy Journal*, 32(1), 30-36. <https://doi.org/10.1097/cpt.0000000000000167>
- Gurovich, A. N., Rodriguez, L., & Morales-Acuna, F. (2021, Nov). There are no differences in brachial artery endothelial shear stress and blood flow patterns between males and females during exercise. *Clin Physiol Funct Imaging*, 41(6), 471-479. <https://doi.org/10.1111/cpf.12722>
- Hambrecht, R., Wolf, A., Gielen, S., Linke, A., Hofer, J., Erbs, S., Schoene, N., & Schuler, G. (2000, Feb 17). Effect of exercise on coronary endothelial function in patients with coronary artery disease. *N Engl J Med*, 342(7), 454-460. <https://doi.org/10.1056/nejm200002173420702>
- Hamburg, N. M., McMackin, C. J., Huang, A. L., Shenouda, S. M., Widlansky, M. E., Schulz, E., Gokce, N., Ruderman, N. B., Keaney, J. F., Jr., & Vita, J. A. (2007, Dec). Physical inactivity rapidly induces insulin resistance and microvascular dysfunction in healthy volunteers. *Arterioscler Thromb Vasc Biol*, 27(12), 2650-2656. <https://doi.org/10.1161/atvbaha.107.153288>
- Harris, R. A., Nishiyama, S. K., Wray, D. W., & Richardson, R. S. (2010). Ultrasound assessment of flow-mediated dilation. *Hypertension*, 55(5), 1075-1085.

- Haynes, A., Linden, M. D., Chasland, L. C., Nosaka, K., Maiorana, A., Dawson, E. A., Dembo, L. H., Naylor, L. H., & Green, D. J. (2017, Jun 1). Acute impact of conventional and eccentric cycling on platelet and vascular function in patients with chronic heart failure. *J Appl Physiol (1985)*, *122*(6), 1418-1424. <https://doi.org/10.1152/jappphysiol.01057.2016>
- Higashi, Y., Sasaki, S., Kurisu, S., Yoshimizu, A., Sasaki, N., Matsuura, H., Kajiyama, G., & Oshima, T. (1999, Sep 14). Regular aerobic exercise augments endothelium-dependent vascular relaxation in normotensive as well as hypertensive subjects: role of endothelium-derived nitric oxide. *Circulation*, *100*(11), 1194-1202. <https://doi.org/10.1161/01.cir.100.11.1194>
- Hortobágyi, T., Barrier, J., Beard, D., Braspeninx, J., Koens, P., Devita, P., Dempsey, L., & Lambert, J. (1996, Oct). Greater initial adaptations to submaximal muscle lengthening than maximal shortening. *J Appl Physiol (1985)*, *81*(4), 1677-1682. <https://doi.org/10.1152/jappl.1996.81.4.1677>
- Kingwell, B. A. (2000, Sep). Nitric oxide-mediated metabolic regulation during exercise: effects of training in health and cardiovascular disease. *Faseb j*, *14*(12), 1685-1696. <https://doi.org/10.1096/fj.99-0896rev>
- Knuttgen, H. G., Patton, J. F., & Vogel, J. A. (1982, Sep). An ergometer for concentric and eccentric muscular exercise. *J Appl Physiol Respir Environ Exerc Physiol*, *53*(3), 784-788. <https://doi.org/10.1152/jappl.1982.53.3.784>
- Ku, D. N. (1997). BLOOD FLOW IN ARTERIES. *Annual Review of Fluid Mechanics*, *29*(1), 399-434. <https://doi.org/10.1146/annurev.fluid.29.1.399>
- Leung, F. P., Yung, L. M., Laher, I., Yao, X., Chen, Z. Y., & Huang, Y. (2008). Exercise, vascular wall and cardiovascular diseases: an update (Part 1). *Sports Med*, *38*(12), 1009-1024. <https://doi.org/10.2165/00007256-200838120-00005>
- Libby, P., Ridker, P. M., & Maseri, A. (2002, Mar 5). Inflammation and atherosclerosis. *Circulation*, *105*(9), 1135-1143. <https://doi.org/10.1161/hc0902.104353>
- Manson, J. E., Greenland, P., LaCroix, A. Z., Stefanick, M. L., Mouton, C. P., Oberman, A., Perri, M. G., Sheps, D. S., Pettinger, M. B., & Siscovick, D. S. (2002, Sep 5). Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med*, *347*(10), 716-725. <https://doi.org/10.1056/NEJMoa021067>
- Mattu, A. T., Iannetta, D., MacInnis, M. J., Doyle-Baker, P. K., & Murias, J. M. (2020, Mar). Menstrual and oral contraceptive cycle phases do not affect submaximal and maximal exercise responses. *Scand J Med Sci Sports*, *30*(3), 472-484. <https://doi.org/10.1111/sms.13590>

- Morales-Acuna, F., Ochoa, L., Valencia, C., & Gurovich, A. N. (2019, Jul). Characterization of blood flow patterns and endothelial shear stress during flow-mediated dilation. *Clin Physiol Funct Imaging*, 39(4), 240-245. <https://doi.org/10.1111/cpf.12564>
- O'Connor, G. T., Buring, J. E., Yusuf, S., Goldhaber, S. Z., Olmstead, E. M., Paffenbarger, R. S., Jr., & Hennekens, C. H. (1989, Aug). An overview of randomized trials of rehabilitation with exercise after myocardial infarction. *Circulation*, 80(2), 234-244. <https://doi.org/10.1161/01.cir.80.2.234>
- O'Rourke, M. F., & Nichols, W. W. (2005, Apr). Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension. *Hypertension*, 45(4), 652-658. <https://doi.org/10.1161/01.HYP.0000153793.84859.b8>
- Oldridge, N. B., Guyatt, G. H., Fischer, M. E., & Rimm, A. A. (1988, Aug 19). Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. *Jama*, 260(7), 945-950.
- Parker, B. A., Trehearn, T. L., & Meendering, J. R. (2009, Oct). Pick your Poiseuille: normalizing the shear stimulus in studies of flow-mediated dilation. *J Appl Physiol* (1985), 107(4), 1357-1359. <https://doi.org/10.1152/jappphysiol.91302.2009>
- Peacock, J., Jones, T., Tock, C., & Lutz, R. (1998). The onset of turbulence in physiological pulsatile flow in a straight tube. *Experiments in fluids*, 24(1), 1-9.
- Peñailillo, L., Blazeovich, A., & Nosaka, K. (2014, Apr). Energy expenditure and substrate oxidation during and after eccentric cycling. *Eur J Appl Physiol*, 114(4), 805-814. <https://doi.org/10.1007/s00421-013-2816-3>
- Peñailillo, L., Blazeovich, A., Numazawa, H., & Nosaka, K. (2013, Sep). Metabolic and muscle damage profiles of concentric versus repeated eccentric cycling. *Med Sci Sports Exerc*, 45(9), 1773-1781. <https://doi.org/10.1249/MSS.0b013e31828f8a73>
- Perrey, S., Betik, A., Candau, R., Rouillon, J. D., & Hughson, R. L. (2001, Nov). Comparison of oxygen uptake kinetics during concentric and eccentric cycle exercise. *J Appl Physiol* (1985), 91(5), 2135-2142. <https://doi.org/10.1152/jappphysiol.2001.91.5.2135>
- Rakobowchuk, M., Ritter, O., Wilhelm, E. N., Isacco, L., Bouhaddi, M., Degano, B., Tordi, N., & Mourot, L. (2017, Apr 1). Divergent endothelial function but similar platelet microvesicle responses following eccentric and concentric cycling at a similar aerobic power output. *J Appl Physiol* (1985), 122(4), 1031-1039. <https://doi.org/10.1152/jappphysiol.00602.2016>
- Ratcliffe, B., Pawlak, R., Morales, F., Harrison, C., & Gurovich, A. N. (2017). Internal validation of an automated system for brachial and femoral flow mediated dilation. *Clin Hypertens*, 23, 17. <https://doi.org/10.1186/s40885-017-0073-1>

- Simon, A. C., Levenson, J., & Flaud, P. (1990, Feb). Pulsatile flow and oscillating wall shear stress in the brachial artery of normotensive and hypertensive subjects. *Cardiovasc Res*, 24(2), 129-136. <https://doi.org/10.1093/cvr/24.2.129>
- Sonka, M., Liang, W., & Lauer, R. M. (2002, Oct). Automated analysis of brachial ultrasound image sequences: early detection of cardiovascular disease via surrogates of endothelial function. *IEEE Trans Med Imaging*, 21(10), 1271-1279. <https://doi.org/10.1109/tmi.2002.806288>
- Stacy, M. R. (2011). *The effect of eccentric exercise-induced muscle injury on vascular function and muscle blood flow*. The University of Toledo.
- Stacy, M. R., Bladon, K. J., Lawrence, J. L., McGlinchy, S. A., & Scheuermann, B. W. (2013, Dec). Serial assessment of local peripheral vascular function after eccentric exercise. *Appl Physiol Nutr Metab*, 38(12), 1181-1186. <https://doi.org/10.1139/apnm-2012-0448>
- Thomas, G. D. (2015, Mar). Functional sympatholysis in hypertension. *Auton Neurosci*, 188, 64-68. <https://doi.org/10.1016/j.autneu.2014.10.019>
- Thomas, G. D., & Segal, S. S. (2004, Aug). Neural control of muscle blood flow during exercise. *J Appl Physiol (1985)*, 97(2), 731-738. <https://doi.org/10.1152/jappphysiol.00076.2004>
- Tsao, C. W., Aday, A. W., Almarzooq, Z. I., Alonso, A., Beaton, A. Z., Bittencourt, M. S., Boehme, A. K., Buxton, A. E., Carson, A. P., Commodore-Mensah, Y., Elkind, M. S. V., Evenson, K. R., Eze-Nliam, C., Ferguson, J. F., Generoso, G., Ho, J. E., Kalani, R., Khan, S. S., Kissela, B. M., Knutson, K. L., Levine, D. A., Lewis, T. T., Liu, J., Loop, M. S., Ma, J., Mussolino, M. E., Navaneethan, S. D., Perak, A. M., Poudel, R., Rezk-Hanna, M., Roth, G. A., Schroeder, E. B., Shah, S. H., Thacker, E. L., VanWagner, L. B., Virani, S. S., Voecks, J. H., Wang, N. Y., Yaffe, K., & Martin, S. S. (2022, Feb 22). Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. *Circulation*, 145(8), e153-e639. <https://doi.org/10.1161/CIR.0000000000001052>
- Vanhoutte, P. M., Shimokawa, H., Tang, E. H., & Feletou, M. (2009, Jun). Endothelial dysfunction and vascular disease. *Acta Physiol (Oxf)*, 196(2), 193-222. <https://doi.org/10.1111/j.1748-1716.2009.01964.x>
- VanTeeffelen, J. W., & Segal, S. S. (2003, Jul 15). Interaction between sympathetic nerve activation and muscle fibre contraction in resistance vessels of hamster retractor muscle. *J Physiol*, 550(Pt 2), 563-574. <https://doi.org/10.1113/jphysiol.2003.038984>
- Virani, S. S., Alonso, A., Aparicio, H. J., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Cheng, S., Delling, F. N., Elkind, M. S. V., Evenson, K. R., Ferguson, J. F., Gupta, D. K., Khan, S. S., Kissela, B. M., Knutson, K. L., Lee, C. D., Lewis, T. T., Liu, J., Loop, M. S., Lutsey, P. L., Ma, J., Mackey, J., Martin, S. S., Matchar, D. B., Mussolino, M. E., Navaneethan, S. D., Perak, A. M., Roth, G. A., Samad, Z., Satou, G. M., Schroeder, E. B., Shah, S. H., Shay, C. M., Stokes, A., VanWagner, L.

B., Wang, N. Y., & Tsao, C. W. (2021, Feb 23). Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. *Circulation*, *143*(8), e254-e743. <https://doi.org/10.1161/cir.0000000000000950>

Vlachopoulos, C. (2005). McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles. *Hodder Arnold*(2005).

Warburton, D. E., & Bredin, S. S. (2016, Apr). Reflections on Physical Activity and Health: What Should We Recommend? *Can J Cardiol*, *32*(4), 495-504. <https://doi.org/10.1016/j.cjca.2016.01.024>

Zhao, G., Li, C., Ford, E. S., Fulton, J. E., Carlson, S. A., Okoro, C. A., Wen, X. J., & Balluz, L. S. (2014, Feb). Leisure-time aerobic physical activity, muscle-strengthening activity and mortality risks among US adults: the NHANES linked mortality study. *Br J Sports Med*, *48*(3), 244-249. <https://doi.org/10.1136/bjsports-2013-092731>

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