ABSTRACT

EFFECTS OF DIFFERENT EXERCISE MODALITIES ON POSTPRANDIAL VASCULAR ENDOTHELIAL FUNCTION IN OVERWEIGHT AND OBESE ADULTS

by Conlan Jarrett Varty

Postprandial hyperglycemia (PPH) impairs vascular endothelial function (VEF) and increases cardiovascular disease risk. A single bout of aerobic exercise (AE) attenuates PPH-induced decreases in brachial artery flow-mediated dilation (FMD), a non-invasive measure of VEF, in healthy adults for up to 17 hours post-exercise. Studies examining the effects of acute resistance exercise (RE) on postprandial FMD responses are lacking. The purpose of this investigation was to determine the effects of different exercise modalities on brachial artery FMD and plasma glucose and insulin responses to an oral glucose tolerance test (OGTT) in overweight and obese adults. We hypothesized that a single bout of exercise performed the prior evening would attenuate PPH-mediated decreases in FMD, independent of exercise modality. In a randomized, crossover design, overweight and obese adults [n = 11 (8 women); age = 21.8 ± 3.8 y; BMI = 32.3 ± 5.8 kg/m²] completed three separate trials. Seated rest (control), 30 min of AE, or 30 min of whole-body RE preceded an OGTT by 14-17 hours. Brachial artery FMD and plasma glucose and insulin were measured prior to and at 30 min intervals for 2 hours following the OGTT. Repeated-measures ANOVA and Bonferroni post-hoc tests were used to evaluate differences within and between trials. A main effect due to time (P<0.001) was observed for FMD. Relative to baseline, brachial artery FMD transiently decreased (P<0.01) at 30-60 min post-ingestion. A main effect due to time (P<0.01) was observed for plasma glucose and insulin. Relative to baseline, glucose increased (P<0.01) at 30-90 min post-ingestion and insulin increased (P<0.05) at 30-120 min post-ingestion. No between trial differences were observed for brachial artery FMD, glucose, or insulin. CONCLUSION: Acute aerobic or resistance exercise performed the evening prior to an OGTT does not attenuate postprandial decreases in brachial artery FMD in overweight and obese adults.
This Thesis titled
EFFECTS OF DIFFERENT EXERCISE MODALITIES ON POSTPRANDIAL VASCULAR FUNCTION IN OVERWEIGHT AND OBESE ADULTS
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Chapter 1
Introduction

Individuals spend a large proportion of their day in a postprandial state, defined as the time period following the ingestion of a meal that lasts approximately 4-6 hours. Epidemiological data suggest that postprandial hyperglycemia (PPH), the elevation of blood glucose levels following an oral glucose challenge/high-carbohydrate meal, better predicts cardiovascular disease (CVD)-related mortality compared to fasting blood glucose levels [1]. Human studies support that PPH increases CVD risk, in part, by transiently impairing vascular endothelial function (VEF) [2]. Brachial artery flow mediated-dilation (FMD), the dilatory response to an increase in blood flow (i.e., vascular shear stress), is a standard non-invasive technique for assessing VEF that reflects nitric oxide (NO) dependent dilation [3, 4] and predicts future CVD risk [5, 6]. PPH transiently decreases brachial artery FMD in healthy adults [7], individuals with impaired glucose tolerance [8], and type 2 diabetics [8]. Increased oxidative stress and reduced bioavailability of the vasodilator NO are suggested to contribute to PPH-induced impairment of VEF [2]. Thus, strategies that lower PPH may prevent impairment of VEF and reduce CVD risk.

Acute moderate-intensity aerobic exercise (AE) decreases postprandial blood glucose levels for up to 3 days post-exercise [9]. Further, a single bout of AE has been shown to attenuate PPH-induced decreases in brachial artery FMD for up to 17 hours post-exercise in healthy adults [10], suggesting that acute AE lessens the adverse effects of PPH on VEF. Studies examining the effect of prior resistance exercise (RE) on postprandial blood glucose responses are less conclusive, with most [11-13], but not all [14], studies showing no effect of prior (i.e., 14-24 hours) RE. To our knowledge, no studies have evaluated the impact of an acute bout of RE on PPH-induced changes in VEF. Further, no studies have examined the effects of acute exercise on postprandial FMD responses in overweight and obese adults, a condition that afflicts over 70% of the U.S. adults [15] and is associated with exaggerated PPH responses [16] and increased CVD risk [17].

The purpose of this investigation was to determine if acute exercise attenuated PPH-induced impairment of VEF in overweight and obese adults. Additionally, we sought to determine whether differences existed between exercise modalities. Compared to a non-exercise
control condition, we hypothesized that a single bout of AE or RE performed 14-17 hours prior to an oral glucose tolerance test (OGTT) would attenuate PPH-induced decreases in brachial artery FMD, independent of exercise modality. Our anticipated findings are timely and of public significance given the increasing prevalence of overweight and obesity [15, 18]. Further, findings from this study will provide preliminary data for future studies to determine the efficacy of various lifestyle strategies to attenuate postprandial metabolic disturbances in clinical populations.
Chapter 2

Literature Review

Overview: Review of the pertinent literature on this topic is divided into five related categories: 1) Measures of VEF; 2) Relationship between VEF and CVD risk; 3) PPH impairs VEF 4) Overweight and obesity impairs VEF and increases CVD risk; and 5) Acute exercise, PPH, and VEF.

1) Measures of VEF

A single layer of endothelial cells exist on the interior lining of the body’s vascular system. In order to maintain homeostasis within the vascular system, endothelial cells respond to stimuli such as increased blood flow, and release chemicals that cause vasodilation or vasoconstriction. Nitric oxide (NO) released by endothelial cells in response to blood flow-induced shear stress induces vasodilation [19]. NO exerts its anti-atherosclerotic role on the vasculature by relaxing smooth muscle cells and by preventing adhesion of platelets and leukocytes, and expression of adhesion molecules [20]. A non-invasive measure of shear stress on the lumen of the vasculature is shear rate [21]. Shear rate is the change in velocity as one layer of a fluid flows over an adjacent layer. In humans, evidence suggests that increased shear stress leads to vasodilation induced by NO release from the endothelium [22]. Figure 1 shows how shear stress initiates the production of NO from the endothelium.

Common methods to assess VEF include conduit artery flow-mediated dilation (FMD) [4], iontophoresis, and venous occlusion plethysmography [23]. These techniques all utilize different degrees of invasiveness to measure VEF. Arterial flow-mediated dilation (FMD) is a noninvasive technique that utilizes high-resolution ultrasound imaging. Brachial artery FMD reflects dilation that is dependent on NO production [3]. The arterial FMD technique uses an inflatable cuff applied to the limb distal to the ultrasound probe and set to a suprasystolic pressure (e.g., 200-250 mmHg) for a period of 5 minutes to induce temporary ischemia and dilation of downstream vessels. Upon release of the cuff, a brief period of reactive hyperemia occurs which stimulates arterial dilation [21]. Changes in blood velocity and arterial diameter relative to resting measurements are used to calculate reactive hyperemia-induced shear stress and vasodilation, respectively. Brachial artery FMD predicts risk of future CVD events, and is often considered alongside other more traditional CVD risk factors [5].
Figure 1. The figure below depicts the cellular pathway that leads to the production of NO in endothelial cells. Blood flow-induced shear stress deforms the shape of the endothelial cells, leading to the production and release of NO from endothelial cells. NO induces vasodilation of the artery by relaxing the surrounding vascular smooth muscle [4].

2) Relationship Between VEF and CVD risk

Cardiovascular disease is the leading cause of the death in the United States for both men and women [18]. Vascular endothelial dysfunction, defined as a reduction in endothelium-dependent vasodilation, is a contributing factor to CVD that promotes atherosclerosis [24-26]. Epidemiological data suggest that impaired VEF is associated with a greater incidence of CVD [6] and is closely associated with traditional CVD risk factors, including age, obesity, hypertension, and diabetes [27, 28]. In a case-cohort subset of the Multi-Ethnic Study of Atherosclerosis (MESA), brachial artery FMD was a predictor of incident cardiovascular events in adults free of CVD at baseline [5]. In the presence of CVD risk factors, structural and functional changes occur in the endothelium that cause a loss of its vasoprotective properties [29]. The primary alteration to the endothelium is the impairment of NO bioavailability, either
because of limited production by endothelial nitric oxide synthase (eNOS) or increased breakdown by reactive oxygen species (ROS) [20]. Strategies to prevent/attenuate vascular endothelial dysfunction may reduce CVD risk.

3) **Postprandial Hyperglycemia (PPH) Impairs VEF**

The postprandial period is the time directly following consumption of a meal, and individuals spend the majority of their day in this state. Epidemiological data suggest that postprandial hyperglycemia (PPH), the elevation of blood glucose levels due to ingestion of a high-carbohydrate meal, better predicts future CVD-related mortality than fasting glucose levels [1].

Studies show that PPH transiently decreases brachial artery FMD in healthy adults [2, 7, 8, 30]. In one such study, an inverse relationship between FMD and plasma glucose was demonstrated, with maximum reduction of FMD coinciding with peak blood glucose levels [7]. Several mechanisms may explain why PPH induces vascular endothelial dysfunction. One of these mechanisms is the production of ROS [8], which are produced through several pathways, including inflammation due to the presence of CVD risk factors, production by the mitochondria during metabolism, and eNOS uncoupling [31]. Along with decreasing NO bioavailability, increased ROS due to hyperglycemia induces lipid peroxidation, reducing eNOS activity that leads to vascular endothelial dysfunction and increased CVD risk [8, 32]. Furthermore, ROS decreases the availability of arginine, the amino acid required for production of NO [7], by reducing the activity of the enzyme dimethylarginine dimethylaminohydrolase (DDAH). DDAH is responsible for degrading asymmetric dimethylarginine (ADMA), a competitive inhibitor of eNOS [33].

4) **Overweight and Obesity Impairs VEF and Increases CVD Risk**

According to the National Institute of Health, over 70% of adults in the U.S. are considered to be overweight or obese [15]. Compared to non-obese adults, overweight and obese individuals have a greater CVD risk [18] that is explained, in part, by lower brachial artery FMD responses [34], greater oxidative stress [35], and exaggerated PPH responses [36]. Impaired glucose tolerance is a period preceding overt diabetes and is characterized by an exaggerated blood glucose response to a carbohydrate load. Being overweight or obese is closely associated with both impaired glucose tolerance and insulin resistance [37-39]. As mentioned previously, PPH transiently decreases brachial artery FMD in healthy adults [7], those with impaired glucose tolerance [8], type 2 diabetes [8], and obese individuals with metabolic syndrome [40]. The rate
of obesity is rising within the United States [41]. Thus, it is important to determine the efficacy of lifestyle strategies, such as exercise, to counteract the detrimental changes in cardiometabolic health in obese individuals.

5) **Acute Exercise, PPH, and VEF**

Regular exercise decreases the risk of CVD, diabetes mellitus, and all-cause mortality [42]. The current recommendation for adults from the American College of Sports Medicine (ACSM) is to engage in at least 30 minutes of moderate-intensity AE 5 days a week, or 20 minutes of vigorous-intensity AE 3 days a week, in addition to 2-3 sessions/week of RE [42]. Both acute and chronic AE have been shown to improve glucose tolerance and insulin sensitivity [43]. Studies show that PPH levels are reduced by acute AE [9, 10], possibly due to an exercise-induced increase in blood flow that promotes glucose delivery and uptake into tissues. However, results from studies examining the effects of RE on PPH and insulin sensitivity are less conclusive [10-12, 14].

**Aerobic Exercise**: Few studies have examined the effect of acute AE on PPH and FMD. In one study, 13 healthy men and women performed two separate trials during which a high-carbohydrate meal was ingested. One trial consisted of a non-exercise control after 48 hours with no exercise, while the other involved 60 minutes of moderate-intensity AE performed 17 hours prior to the consumption of the high-carbohydrate meal. Brachial artery FMD and blood samples were taken every 30 minutes for 2.5 hours after consumption of the high-carbohydrate meal. Compared to the non-exercise control trial, postprandial plasma glucose AUC was shifted downwards, while postprandial decreases in brachial artery FMD were attenuated by prior AE.

In a separate study, 11 healthy young men (age = 22.6 ± 2.3) completed two separate trials: one trial consisted of seated rest following ingestion of a 75 g OGTT; with a separate trial consisted of 45 min of moderate-intensity AE performed immediately following glucose ingestion [44]. Brachial artery FMD and venous blood samples were taken every hour for 4 hours. In the non-exercise trial, postprandial FMD significantly decreased at 1-hour post ingestion. While plasma glucose concentrations did not significantly differ between trials, there was no postprandial decrease in FMD when acute exercise followed the OGTT, suggesting that performing acute AE immediately following a glucose challenge attenuates PPH-induced impairments in VEF.
Resistance Exercise: In contrast to AE, data regarding the effect of acute RE on PPH are less convincing. In one study, 10 healthy strength-trained men performed an acute bout of RE approximately 14 hours before the ingestion of a carbohydrate-rich meal (1 g/kg of body weight) [14]. Venous blood samples were taken every 15 minutes for 2 hours after meal consumption. Although RE did not significantly lower postprandial blood glucose and plasma insulin levels when compared to a non-exercise control, peak plasma glucose and incremental area under the blood glucose curve in the period 0-60 min were significantly lower after performing RE [14]. In another study examining the effects of a single bout of resistance exercise on insulin sensitivity and glucose tolerance in three different groups- young control subjects, older patients with non-insulin-dependent diabetes mellitus (NIDDM), and older age-matched control subjects-participants first completed a pre-OGTT, followed 48 h later by a resistance exercise bout consisting of 7 exercises, and again followed by a post-OGTT 18 h later. There were no changes found between pre and post glucose levels in any of the groups, however, the total insulin responses (AUC) of the young control and NIDDM groups were significantly lower after exercise. In contrast, multiple studies have also found that a single bout of RE performed does not significantly alter postprandial plasma glucose or insulin responses. One study in overweight postmenopausal women (58 y, BMI = 27 kg/m²) showed that an acute bout of RE performed 15 hours before an intravenous glucose tolerance test did not influence measures of glucose tolerance or insulin sensitivity [11]. In a separate cross-over study, 10 obese men (BMI >30 kg/m²) performed 3 separate trials the day before a 100 g OGTT: an AE trial consisting of 60 min of cycling at 70% VO₂peak, a 60 min RE trial consisting of 8 whole-body exercises with 2 sets of 8 reps and a third set to fatigue at 80% 1 rep max, and a 60 minute non-exercise control trial [12]. No significant differences were found between trials for postprandial plasma glucose or insulin responses. To our knowledge, no studies have examined the effect of acute RE on PPH-induced changes in VEF in overweight and obese adults.

Collectively, previous studies support that acute AE lowers PPH and attenuates PPH-induced impairment of VEF in healthy adults. Studies are needed in clinical populations to determine the efficacy of different exercise modalities to attenuate postprandial impairment of VEF and reduce CVD risk.

Purpose Statement and Hypothesis: The primary purpose of this investigation was to determine if an acute bout of exercise performed 14-17 hours prior to an oral glucose load
attenuates PPH-induced impairment of VEF in overweight and obese adults. Additionally, we sought to determine whether differences existed between exercise modalities. Compared to a non-exercise control condition, we hypothesized that a single bout of AE or RE performed 14-17 hours prior to an OGTT would attenuate PPH-induced decreases in brachial artery FMD, independent of exercise modality.
Chapter 3
Methodology

Study design: The protocol for this study was approved by the Institutional Review Board at Miami University and written informed consent was obtained from all participants. Participants completed three randomized trials in a crossover design: 1) 30 min of acute AE, 2) 30 min of acute RE, and 3) a control (non-exercise) trial. Each trial consisted of two separate visits to the laboratory. Following the first visit in the late afternoon/early evening, participants left the laboratory and returned the next morning (14-17 h later) after an overnight fast (>10 h). During each morning visit, brachial artery FMD was assessed and blood collected prior to and at 30 min intervals for 2 h following the ingestion of an OGTT (Figure 2). Participants were instructed to maintain their current physical activity habits throughout the study. Participants were also instructed to keep a diary of all food consumed for the day preceding the initial OGTT, and to replicate this diet for the day prior to the two subsequent OGTT trials.

Figure 2. Timeline of study design. FMD, flow mediated dilation. OGTT, oral glucose tolerance test.

Subjects: Eleven (n = 11) overweight or obese men and women (BMI≥25.0 kg/m²) were recruited to participate in this study. Inclusion criteria included: 18-50 y of age, non-smokers, BMI≥25.0 kg/m², alcohol intake <3 drink per day or <10 drinks per week, not taking any
medications for hypertension, high cholesterol, or diabetes, no dietary supplements, no musculoskeletal injuries or physical limitations, no history or symptoms of pulmonary, cardiovascular, metabolic, or neurological disease, and <2 d/week of moderate-intensity physical activity over the past 6 months.

**Dietary Control:** Participants completed a 1 d food log prior to their first study trial and instructed to replicate their dietary intake the day prior to their second and third trials. Food records were assessed for energy and nutrient intake (Food Processor Nutrition Analysis software, version 11.2, ESHA Research, Salem, OR, USA).

**Screening Visit:** Subjects were instructed to arrive at the laboratory following an overnight fast and no exercise for 48 h. After informed consent was obtained, height, weight, body composition via bioelectrical impedance analysis (InBody 770, Cerritos, CA, USA), waist circumference, and resting blood pressure and heart rate were obtained. Next, health history and physical activity questionnaires were completed. The International Physical Activity Questionnaire (IPAQ) was used to determine each subject’s habitual physical activity levels. Women completed a questionnaire at the screening visit and at each trial to assess their menstrual history and oral contraceptive use [45, 46] and to ensure that they were tested at approximately the same phase of their individual menstrual cycle. A fasted blood sample was obtained from an antecubital vein for the determination of blood glucose and lipids (Cholestech). Lastly, subjects completed a VO$_2$max test on a treadmill using open circuit spirometry (ParvoMedics, Sandy, UT, USA) to determine maximal oxygen uptake. In order to be considered a true max test, subjects had to meet at least 3 out of these 4 criteria: 1.) Plateau in oxygen consumption, 2.) HR ± 10 bpm of age-predicted max, 3.) Respiratory exchange ratio (RER) of 1.1 or higher, 4.) 18 or higher on the Borg Scale for Rating of Perceived Exertion (RPE) [47].

**Familiarization Visit:** Participants returned to the laboratory approximately 1 week later to become familiarized with the RE equipment, and to determine their 10-repetition maximum (10-RM) for the following exercises: seated leg press, seated chest press, seated leg curl, lat pulldown, seated shoulder press, and seated row. Following a 5 min warm-up on the treadmill, each participant’s 10-RM was determined. The 10-RM protocol consisted of a set of 10 repetitions with a light load, followed by the participant performing successive sets with increasing loads until study personnel determined the 10-RM load. Each participant’s 10-RM load was determined within 3-5 sets.
Testing Trials: Approximately 1 week after the completion of the familiarization visit, subjects returned to the laboratory in the late afternoon/early evening following a 2 h fast and no exercise for 48 h. The three trials were separated by ≥1 wk in men and approximately 1 month in women to account for fluctuations in brachial artery FMD that occur throughout the menstrual cycle [48].

1. No Exercise Trial (control): Participants sat quietly in the laboratory for 40 min.

2. AE Trial: Participants performed a 5 min warm-up on the treadmill at a self-selected pace, followed by 30 minutes of moderate-intensity AE at 50-60% VO2max. Oxygen uptake was constantly measured using open circuit spirometry during the first 15 minutes of exercise to determine the participant was at the prescribed intensity. The speed and/or grade of the treadmill was adjusted if oxygen uptake was not within ±5% of the desired intensity. A 5 min cooldown concluded the AE bout.

3. RE Trial: Participants performed a 5 min warm-up on the treadmill at a self-selected pace, followed by 3 sets of 10 repetitions for the six selected exercises. The load used for each exercise was the participant’s previously determined 10-RM. Participants rested 90 sec between sets and 120 sec between exercises. A 5 min cooldown concluded the aerobic exercise bout. The RE bout, not including the warm-up and cooldown period, lasted approximately 30 min.

Heart rate and RPE were assessed at rest, at 10 min intervals during the control trial, at 5 min intervals during AE trial, and following each set during the RE trial. Participants reported back to the laboratory the next morning (14-17 later) after an overnight fast.

OGTT: At the morning visit, body mass and composition were assessed using bioelectrical impedance analysis (InBody). Next, brachial artery FMD was assessed following 15 min of supine rest. Following the assessment of baseline FMD, an intravenous catheter was inserted into an antecubital vein, and a fasting blood sample was obtained. Participants then ingested the glucose beverage (TRUTOL, Fisher Diagnostics) at a dose of 1 gram of glucose per kg body mass. Brachial artery FMD was assessed and blood samples collected at 30 min intervals during the 2 h postprandial period.

Brachial Artery Flow Mediated Dilation: Brachial artery FMD was assessed using high-frequency ultrasonographic imaging as described [40]. The rapid inflation cuff was placed on the subject’s forearm just distal to the elbow, and the brachial artery was imaged on the upper arm.
using a 5- to 12-MHz multi-frequency linear array transducer connected to a high-resolution ultrasound (uSmart 3300; Terason, Burlington, MA, USA). Pre-occlusion recording of blood velocity and arterial diameter were taken for 1 minute. The cuff was then rapidly inflated to a pressure of 200 mmHg for 5 minutes using a rapid cuff inflator (Hokanson E20, Bellvue, WA, USA), and then quickly released following this period. Blood velocity and arterial diameter were recorded for the last minute of cuff inflation, and for 3 minutes following deflation. Subjects’ skin was marked to ensure identical transducer placement for subsequent measurements. Ultrasound recordings were analyzed using automated edge-detected software with end-diastolic gating (Medical Imaging Applications, Iowa City, IA). Shear rate was calculated from end-diastolic synchronized diameter and velocity data [21]. Shear rate AUC was calculated from the time of cuff release until the time of maximal post-occlusion diameter to determine the hyperemic stimulus responsible for FMD [49].

**Blood Analysis:** Whole blood was collected into tubes coated with EDTA or lithium heparin. Following centrifugation (3000 rpm, 4°C 15 min), plasma was divided and archived at -80°C until analysis. Plasma glucose was measured using a commercially available clinical assay (Pointe Scientific, Canton, MI, USA) on a microplate reader (BioTek Instruments, Synergy HT, Winooski, VT, USA). Plasma insulin was measured using an enzyme-linked immunosorbent assay kit (ALPCO, Salem, NH). Insulin and glucose area under the curve (AUC) were calculated using the trapezoidal method.

**Statistical Analyses:** Sample size for this study was determined utilizing data from previously reported postprandial studies examining changes in brachial artery FMD following the ingestion of an OGTT [46, 50]. Based on these data [46, 50], we calculated that nine participants would provide 80% power to detect changes in brachial artery FMD. One-way ANOVA was used to evaluate between trial differences in fasting measures. Two-way repeated-measures ANOVA were used to evaluate differences due to time, trial, and their interaction. In the presence of significant main or interaction effects, pairwise differences within and between groups were evaluated using Bonferroni post-hoc tests. One-way ANOVA was used to evaluate dietary intake and AUC data between trials. Data are means ± SD unless otherwise indicated. An α-level of P≤0.05 was considered statistically significant for all analyses.
Participants and Dietary Intakes: Eleven (n = 11) (8 females) overweight and obese individuals completed the study (Table 1). Participants were physically inactive (<1 day/week of moderate-intensity physical activity), overweight or obese based on BMI, and had resting blood pressure within normal clinical limits. Dietary intakes of energy and macronutrients did not differ between trials (Table 2), indicating the participants’ maintained similar dietary patterns throughout the study.

Study Trials: Body mass did not differ between trials (97.2 kg, 97.9 kg, and 98.4 kg for trials 1, 2, and 3, respectively; P>0.05). All exercise (and control) trials were performed between 3:00 and 6:00 p.m., which was 15.3 ± 1.0 h prior to the OGTT performed the next morning. Participants completed the 30 min of AE at 58.7 ± 5.5% VO$_2$max (17.9 ± 2.4 ml/kg/min). Average RPE did not differ between the AE and RE trials (12.6 ± 1.8 and 13.5 ± 1.1 for AE and RE, respectively; P>0.05), indicating similar intensity between the acute exercise bouts.

Plasma Glucose and Insulin: Fasting plasma glucose (Figure 3) and insulin (Figure 4) concentrations did not differ between trials. Plasma glucose increased (Time: P<0.001) by 30 min following glucose ingestion and remained elevated from baseline through 90 min (Figure 3). Plasma glucose AUC did not differ between trials (16942 ± 3336 mg/dL/min, 16037 ± 2392 mg/dL/min, and 15837 ± 2566 mg/dL/min for control, AE, and RE, respectively; P≥0.17). Plasma insulin increased (Time: P<0.01) by 30 min following glucose ingestion and remained elevated from baseline through 120 min (Figure 4). Plasma insulin AUC did not differ between trials (13546 ± 12079 µIU/mL/min, 13337 ± 9480 µIU/mL/min, and 11923 ± 7595 µIU/mL/min for control, AE, and RE, respectively; P≥0.13).

Brachial Artery FMD: Pre-occlusion brachial artery diameter did not differ throughout the postprandial period nor between trials (Table 3). Peak brachial artery diameter decreased from baseline at 30 min (P<0.01), with no differences detected between trials (Table 3). Brachial artery FMD responses decreased (P<0.01) from baseline at 30-60 min, with no differences detected between trials (Figure 5). Absolute FMD values showed similar responses. A main
effect for time (P<0.01) was observed for shear rate AUC, but no pairwise differences were detected (Figure 6).

Chapter 5
Discussion

To our knowledge, our study is the first to examine the effect of different exercise modalities on postprandial FMD responses to an OGTT in overweight and obese individuals. Overweight and obese adults were chosen for this study as they are at an increased risk for development of CVD, and make up approximately two-thirds of the U.S. adult population [15]. Additionally, obese individuals exhibit exaggerated PPH responses compared to lean individuals [16], suggesting that acute exercise might attenuate PPH to a greater extent than previous observations in healthy adults [10, 14]. Consistent with prior studies [7, 40], we showed that PPH transiently decreased brachial artery FMD, a measure of VEF that reflects NO dependent dilation [3, 4] and predicts future CVD risk [5, 6]. However, compared to a non-exercise control trial, performing an acute bout of AE or RE approximately 15 hours prior to an OGTT did not attenuate PPH responses or postprandial decreases in brachial artery FMD in our participants.

Few studies have simultaneously evaluated the effects of acute exercise on postprandial metabolic and vascular responses. In one study, 13 healthy men and women (48 y, BMI = 24 kg/m²) consumed a high carbohydrate meal (101 g carbohydrate) on two separate occasions: 17 hours after performing a 60 min bout of AE and after 48 hours with no exercise [10]. Blood samples were collected and brachial artery FMD was assessed at baseline and every 30 minutes for 150 min after consumption of the high carbohydrate meal. Acute AE did not eliminate PPH-induced decreases in brachial FMD, but did shift the FMD response curve upward (treatment: P<0.001). Further, acute AE shifted the postprandial plasma glucose and insulin response curves downward (treatment: P<0.05). These data suggest that performing acute AE the evening prior to a high carbohydrate challenge attenuates PPH-induced decreases in FMD in healthy adults [10].

A separate study in 10 healthy resistance-trained men (24 y, BMI = 24 kg/m²) reported that an acute bout of RE performed 14 hours before consumption of a carbohydrate-rich meal (1 g/kg body mass) did not significantly lower 2-hour postprandial blood glucose or insulin responses compared to a non-exercise control trial [14]. However, peak blood glucose values and incremental area under the blood glucose curve in the period 0-60 min after carbohydrate
ingestion were lower when the carbohydrate-rich meal was preceded by acute RE [14]. Others have shown that acute RE performed 15-18 hours prior to a high-carbohydrate challenge does not significantly attenuate postprandial blood glucose responses [11, 13]. To our knowledge, only one study has determined the effects of prior AE and RE of equal duration on postprandial glucose tolerance in obese individuals. In 10 obese untrained men (24 y, BMI = 33 kg/m²), neither 60 min of AE or 60 min of RE performed 24 hours prior to an 100 g OGTT lowered postprandial blood glucose or insulin responses compared to a non-exercise trial [12]. The present study in overweight and obese adults advances existing knowledge by showing that acute AE or AE matched for duration do not attenuate the adverse effect of PPH on VEF. Studies examining the effects of prior AE and RE on postprandial changes in vascular function are scarce. In 18 middle-aged overweight and obese individuals (59 y; BMI = 32 kg/m²), no significant differences were found in blood glucose AUC responses to a mixed meal challenge (50% carbohydrate, 15% protein, 35% fat) when comparing a non-exercise control condition to three separate acute exercise trials performed 14 hours prior to the meal: 30 minutes of AE, 30 minutes of RE, or 30 minutes of combined exercise [51]. Central augmentation index, a measure of arterial stiffness, decreased postprandially with no differences observed between trials [51]. Interestingly, while insulin AUC levels were not significantly different in any of the exercise trials compared to the non-exercise control condition, insulin AUC was significantly lower following RE compared to AE [51]. In the present study, insulin AUC was lower in the RE trial compared to the AE and control trials, albeit not significantly. Thus, it is possible that acute RE is more effective at improving postprandial insulin sensitivity relative to AE of similar duration, perhaps due to differences in exercise intensity between modalities and/or increased muscle mass utilization during RE. Future research is warranted to determine the effects of different exercise modalities varying in intensity and duration on postprandial cardiometabolic disturbances in clinical populations.

**Limitations and Directions for Future Research:** Studies in humans support that PPH impairs VEF, at least in part, by inducing oxidative stress responses that reduce NO bioavailability [7, 40]. Oxidative stress and NO bioavailability were not measured in the present study as changes in postprandial responses of these variables are dependent on PPH (i.e., glucose AUC) [7], which did not differ between trials. Our sample size was similar to others examining acute exercise on postprandial glucose tolerance and/or VEF [10-14]. One limitation of the
present study is that only young, overweight and obese individuals were tested. Future studies are needed to determine if age, and therefore greater time of excess body mass, influences the effect of acute exercise on postprandial VEF responses. Furthermore, participants in the current study exercised for a shorter duration than healthy subjects in previous studies [9, 10, 14]. We purposefully chose for participants to complete 30 minutes of AE and RE as this meets current ACSM recommendations [42] and is representative of exercise performed by physically-inactive adults. It is unlikely that a longer duration of exercise would have altered our findings as previous studies show that 60 minutes of AE or RE does not affect postprandial blood glucose responses in obese men [12].

**Conclusion:** We found that performing an acute bout of AE or RE approximately 15 hours prior to an OGTT did not significantly attenuate PPH or postprandial decreases in brachial artery FMD in overweight and obese adults. Findings from our study and others [12] suggest that lowering of postprandial increases in blood glucose and attenuated decreases in postprandial VEF by acute AE in healthy subjects [9, 10] does not extend to overweight and obese individuals at increased CVD risk. The reason for these differences between populations remains to be explored. Future research should be conducted to examine the efficacy of various strategies, including the timing of prior exercise and the combination of exercise and dietary alterations, to attenuate the adverse effects of PPH on VEF and CVD risk. Further, future research should examine if the effect of acute exercise on postprandial metabolism is influenced by age, sex, and/or health status.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>21.8 ± 3.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>32.3 ± 5.8</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>39.2 ± 8.8</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>100.2 ± 19.7</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>113 ± 7</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>77 ± 5</td>
</tr>
<tr>
<td>Resting heart rate (bpm)</td>
<td>77 ± 12</td>
</tr>
<tr>
<td>VO₂max (ml/kg/min)</td>
<td>31.7 ± 5.8</td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>173.6 ± 38.4</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>57.5 ± 19.5</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>90.3 ± 33.7</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>118.8 ± 80.2</td>
</tr>
</tbody>
</table>

Data are means ± SD (n = 11). Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; VO₂max, maximal oxygen consumption.
TABLE 2. Participants’ dietary intakes

<table>
<thead>
<tr>
<th>Variable</th>
<th>RE</th>
<th>AE</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy (kcal/d)</td>
<td>2218 ± 843</td>
<td>2153 ± 744</td>
<td>2131 ± 781</td>
</tr>
<tr>
<td>Carbohydrate (%)</td>
<td>44.9 ± 7.1</td>
<td>45.8 ± 7.6</td>
<td>43.5 ± 6.6</td>
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<tr>
<td>Protein (%)</td>
<td>15.8 ± 5.7</td>
<td>15.1 ± 3.8</td>
<td>15.6 ± 4.2</td>
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<tr>
<td>Fat (%)</td>
<td>38.7 ± 6.7</td>
<td>38.3 ± 6.3</td>
<td>39.8 ± 5.2</td>
</tr>
<tr>
<td>Saturated Fat (g/d)</td>
<td>32.4 ± 16.6</td>
<td>30.2 ± 12.2</td>
<td>30.2 ± 13.4</td>
</tr>
<tr>
<td>Cholesterol (mg/d)</td>
<td>221.1 ± 158.6</td>
<td>201.0 ± 155.4</td>
<td>205.3 ± 158.7</td>
</tr>
</tbody>
</table>

Data are means ± SD, n = 11. Abbreviations: RE, resistance exercise; AE, aerobic exercise. Dietary intakes were determined from food records collected 1-day preceding each trial. Nutrient intakes were analyzed using Food Processor software (ESHA Research, Salem, OR, USA). No differences were detected between trials.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Pre-Occlusion Diameter (mm)</th>
<th>0 min</th>
<th>30 min*</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
<th>150 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time x Trial</td>
<td></td>
<td></td>
<td>0.65</td>
<td>0.67</td>
<td>0.69</td>
<td>0.70</td>
<td>0.72</td>
<td>0.75</td>
</tr>
<tr>
<td>Pre-Occlusion Diameter (mm)</td>
<td></td>
<td></td>
<td>0.67</td>
<td>0.69</td>
<td>0.70</td>
<td>0.72</td>
<td>0.75</td>
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<td></td>
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<td>0.65</td>
<td>0.67</td>
<td>0.69</td>
<td>0.70</td>
<td>0.72</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Data are mean ± SD, n = 11, *p < 0.01 from 0 min.

**TABLE 3. Changes in brachial artery diameter**
Figure 3. Plasma glucose responses for the control and exercise trials. Data are means ± SE.

*P<0.01 from 0.
Figure 4. Plasma insulin responses for the control and exercise trials. Data are means ± SE.

*P<0.05 from 0.
Figure 5. Brachial artery FMD responses for the control and exercise trials (n = 11; data are means ± SE). *P<0.01 from 0.
Figure 6. Shear rate area under the curve (AUC) responses for the control and exercise trials (n = 11; data are means ± SE). P = 0.001, 0.97, and 0.94 for time, trial, and interaction, respectively.
References


