THE EFFECTS OF ISOMETRIC EXERCISE ON IMMEDIATE POST-ISOMETRIC EXERCISE GLUCOSE TOELRANCE

by

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ABSTRACT

SPENCER ANDERSON GREEN. The effects of isometric exercise on immediate post-isometric exercise glucose tolerance. (Under the direction of Dr. REUBEN HOWDEN, Ph.D.)

Dynamic exercise has been shown to improve glucose tolerance. However, it's unclear if isometric exercise produces a similar benefit. The purpose of this study was to observe if an isometric exercise session acutely improved glucose tolerance in 16 apparently healthy males. Males, ages 18-45yrs old, who participated in less than 90 minutes of weekly physical activity were recruited. During session 1, fasting blood glucose, baseline oral glucose tolerance, and bilateral maximum voluntary contraction (MVC) were determined. During session 2 ($\geq$ 24 hours after session 1), fasting blood glucose was assessed followed by consumption for the glucose tolerance beverage. Immediately post consumption, subjects began six, 2-minute contractions at 15% MVC using bilateral quadriceps. Each contraction was separated by 1 minute of rest. Blood glucose was measured at 15, 30, 45, 60, 90, and 120min post drink consumption. Results indicated that one session of isometric exercise did not alter glucose tolerance. Blood glucose was elevated immediately following exercise, which may be due to sympathoadrenal hyperactivity. Our findings suggest that one bout of isometric exercise is not an effective approach to acutely improve glucose tolerance. Future studies should employ isometric exercise training programs in Type II diabetic populations to further investigate potential improvements in glucose tolerance.

DEDICATION

This thesis is dedicated to SGT. David J. Smith, LCPL. Jeremy M. Kane, and HM2. “Doc” Xin Qi in addition to the remaining fallen Marines of Charlie and H&S Company, 4th Light Armored Reconnaissance Battalion, 4th Marine Infantry Division in support of Operation Enduring Freedom.

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CHAPTER 1: INTRODUCTION

Non-Insulin Dependent Diabetes Mellitus (NIDDM) is a metabolic condition characterized by an elevation in hemoglobin A1C (HbA1c), insulin resistance, or abnormalities of insulin production or receptor activity.[29] As a result, the body is unable to efficiently extract glucose from systemic circulation leading to hyperglycemia. Chronic hyperglycemia contributes to chronic inflammation of the vasculature, hypertension, oxidative stress, renal and cardiovascular disease, as well as metabolic syndrome.[6, 7, 9, 26] NIDDM is responsible for an annual mortality rate of 4 million deaths. Additionally, NIDDM is responsible for a global incidence rate of 422 million. Furthermore, NIDDM is contributing to a decline in global health corresponding with a financial burden to global healthcare systems.[1, 18]

Exercise is an efficient therapy for improving glycemic control.[12, 19, 21] Because skeletal muscle is the largest consumer of blood glucose, chronic inactivity may facilitate the loss of lean body mass, resulting in compromised peripheral glucose uptake and insulin sensitivity.[5] Increased concentrations of calcium ions and AMP-activated protein kinase (AMPK) during muscle contractions have been reported to trigger GLUT4 translocation, further eliciting glucose disposal without a substantial presence of insulin.[26, 46] Although the specific physiological mechanisms responsible for exercise induced adaptations to glycemic control remain ambiguous, both dynamic resistance and aerobic exercise have been associated with improvements in beta cell function, insulin sensitivity, glucose clearance capacity, blood lipid profiles, and GLUT4 expression. [1, 5, [7, 17] Furthermore, evidence has also suggested that the protective benefits of exercise are greatest in individuals with the highest risk of NIDDM.[16, 20, 46]

Poor adherence to exercise within NIDDM populations is attributed the fear of hypoglycemic events due to actions of medication, mechanical and breathing discomfort due to obesity, and an insufficiency of proper exercise programming, and cost.[4, 9, 46] Interestingly, it has been reported that there is also a general lack of interest regarding exercise in NIDDM populations within developing countries.[30] However, the exclusion of exercise and the sustainment of sedentary behavior will only exacerbate the condition and perpetually lead the individual to an increased risk for pre-mature mortality.

Isometric exercise training (IET) is a simple and cost-effective modality of exercise that has been determined safe for various populations, including individuals afflicted with cardiovascular disease. Favorably, a great deal of scientific evidence has demonstrated that one bout of isometric exercise as well as programmed IET performed at submaximal intensities has led to clinically significant improvements in health parameters that are associated with cardiovascular disease, such as resting blood pressure.[24, 25, 35, 44, 47, 48] Isometric exercise may be considered a valuable exercise modality simply because it can be performed while resting, there is a lack of considerable physical effort, and it may accommodate one's range of motion if an individual's mobility is limited. Furthermore, it's inexpensive as it requires a handgrip dynamometer, bodyweight or household objects. Following one short bout of isometric handgrip exercise, Van Assche et al.[47] observed significant reductions to resting systolic blood pressure in 15 pre-hypertensive and hypertensive adults. Likewise, Howden et al.[48] observed significant reductions to resting blood pressure following 5 weeks of isometric exercise training using either bilateral leg or arm exercise. More importantly, significant differences in blood pressure between the differing muscle groups were not depicted thus projecting that specific muscle groups do not elicit differing or more favorable outcomes when compared to one another.[48]

Similar to blood pressure responses following one bout of isometric exercise, improvements to blood glucose tolerance (BGT) have been reported following one bout of dynamic resistance exercise in individuals afflicted with impaired glucose tolerance and NIDDM.[17, 18, 45] This important interaction demonstrates a short term effect in which exercise-induced benefits may be obtained without having to implement a training program. As sufficient evidence suggests that aerobic and dynamic resistance exercise improves many parameters associated with human health, limited literature suggests that IET could be an effective approach for improving serum glycemic parameters, thus influencing the risk for NIDDM. [4, 5, 19, 21, 27, 41] Therefore, it is important to assess the efficacy of isometric exercise as a simple and accommodating modality to elicit potential improvements to BGT.

This study is a continuation of pilot data from our laboratory, which found a significantly faster rate of serum glucose disposal in a group of sedentary males after completing one bout of bilateral isometric leg exercise when compared to female counterparts. While considering our pilot data, the overall purpose of this study was to observe if one acute session of isometric exercise could potentially influence BGT verses the implementation of a training program. More importantly, future research regarding IET and any potential influence on BGT may contribute to reductions in dosage or quantity of diabetic medications, vascular complications and comorbidities associated with hypertension and NIDDM, as well as attenuating risk for pre-mature mortality while improving quality of life.[42]

CHAPTER 2: LITERATURE REVIEW

Extensive evidence suggests that NIDDM is associated with an absence of physical activity [18, 19, 21, 23] Those with a fasting blood glucose ≥ 7mmol/L consequently have a 3-fold risk of suffering a cardiovascular event.[1] Thent et al.[30] concluded that 4% of the global population was afflicted with NIDDM in the year of 1995 and is suspected to reach 5.4% by 2025. Within the United States alone, it is currently estimated that 25.8 million are affected with NIDDM and that the annual cost for healthcare treatment for NIDDM exceeds $174 billion.[37]

Although the implementation of anti-hyperglycemic medication has substantially improved glycemic control and reduced mortality rates, non-adherence to medication due to adverse side effects remains a clinical concern.[30, 36] Although hypoglycemia during exercise training has been reported as a common concern with diabetic populations, numerous studies have shown that exercise is a very safe and effective adjunct therapy for NIDDM.[4-11,17, 46] The practice of physical exercise induces a protective role in regards to blood glucose homeostasis but is not well understood. However, it is currently believed that improved blood glucose clearance during exercise occurs as a result of augmented GLUT4 expression, increases in skeletal muscle blood flow, and changes in enzyme activity further improving the physiological parameters of NIDDM.[4, 13, 14, 18, 26, 30] As a result, the practice of habitual exercise and diet restriction in conjunction with pharmacotherapy may contribute to more favorable outcomes rather than medications alone.

Dynamic Resistance Training

Dynamic resistance exercise training induces improvements to insulin sensitivity, lean muscle mass, and bone mineral density.[9, 22] Additionally, resistance exercise training enhances functional status and serves as a protective measure for age-related muscle atrophy.[30] The American Diabetes Association recommends routine strength training as part of a balanced exercise program.[38] Because skeletal muscle is a major reservoir for 90% of blood glucose disposal, it only seems promising that an increase in skeletal muscle surface area will lead to improved blood glucose clearance capacities.[6] Without implementing an exercise protocol, Szczypaczewska et al.[2] demonstrated significant changes to BGT in 10 trained subjects compared to 22 untrained control subjects during a 120-minute oral glucose tolerance test (OGTT). Although the American College of Sports Medicine recommends habitual resistance exercise training in various age groups, it may be especially valuable for elderly populations due to higher rates of NIDDM, skeletal muscle atrophy, and obesity.[14, 35]

Single Resistance Exercise Session Specific to NIDDM Insulin Resistance

While long-term adaptations regarding programmed resistance training and improved glycemic control have been well defined, there is an absence of evidence pertaining to the effectiveness of one acute bout of IET and changes to glycemic control. Regarding programmed resistance training, it has been suggested that improvements in glucose metabolism may result from repeated acute effects, simply because rapid deterioration of glucose tolerance has been seen to occur following the cessation of exercise training.[17]

After 18 hours of completing a single bout of dynamic resistance exercise at 50-75% 1 RM, Fluckey et al.[20] observed no significant improvements in BGT within a cohort of 7 NIDDM males and females. However, following 12-24 hours of one session completion, Fenicchia et al.[17] demonstrated significant improvements to BGT after completing 3 sets of similar resistance exercises at 80% 1 RM within a cohort of 7 NIDDM females. Notably, the observed favorable improvements to BGT were only projected during an acute period and did not persist after 6 weeks of triweekly resistance exercise training.[17] Although both studies utilized control groups and administered 75g glucose beverages, there were significant between-group differences regarding pre-training blood glucose values and body mass index. Also, Flukey and colleagues observed improvements in insulin sensitivity within the NIDDM cohort following one acute bout of exercise, while no change was observed in the ladder.[17, 20] Furthermore, it was also noticed that OGTT durations differed by a 1 hour difference (180 minutes vs 240 minutes).[17, 20] Finally, after treating a young cohort of Wistar rats with Dexamethasone, Araújo et al.[18] elicited a 23% reduction in fasting blood glucose following one resistance exercise session which encompassed 5 sets of 10 squats. Araújo and colleagues successfully demonstrated that one bout of resistance exercise yielded significant improvements to blood glucose parameters while no change was observed in a placebo or control group.

Programmed Resistance Training Specific to NIDDM Populations

Longitudinal studies focusing on the benefits of progressive resistance training and improved glycemic control have been incorporated in NIDDM or familial insulin resistant populations.[3, 14, 16, 14] Although each study design utilized differing exercise programs, populations and training durations, each had a purpose to improve glycemic parameters including BGT in patients diagnosed with NIDDM. Training programs were conducted triweekly, ranging from 9-20 weeks and composed of training intensities of 50-85% maximal heart rate or 1 RM. Furthermore, each implemented a control group or a crossover period of "no training," which served as a reference point for exercise induced adaptations.[3, 16, 31] Although many similarities were discovered in each study, many differences were observed, as well. Smutok et al.[16] yielded a significant 12% reduction in fasting BGT in 8 NIDDM males after 20 weeks of 13 resistance exercises while Maiorana et al.[31] yielded an 18% reduction in BGT in 16 medicated NIDDM males and females following 8 weeks of circuit training consisting of 7 resistance exercises additive with 8 aerobic exercises. Maiorana and colleagues also observed a significant increase in peak VO2.[31] Moreover, there was speculation that 8 weeks of circuit training elicited a reduction in myosin heavy chain (MHC) type IIX isoform while complimenting an increase in MHC IIA, further contributing to improved BGT**.**[3] Erikkson et al.[14] elicited significant improvements to HbA1c additive with a 21% increase to cross-sectional area of the medial vastus lateralis after 12 weeks of resistance exercise training. However, BGT remained unchanged despite a significant increase in LBM surface area.

Although both studies contained short rest periods between exercise sets and obtained similar findings, it was not clear if the subjects used by Smutok and colleagues were medicated for NIDDM.[16] Following 9 weeks of progressive resistance training of the bilateral legs only, Schofield et al.[3] observed noticeable but insignificant attenuations to blood glucose clearence during an OGTT in 7 males and females. Despite the lack of significance, Schofield and colleagues reported that any slight change in fasting blood glucose returned to pre-training values following a 9-week detraining phase.[3] While the present studies utilized small cohorts, it can be concluded that the implementation and maintenance of dynamic resistance training may serve as a useful additive therapy for maintenance and prevention of NIDDM.

Numerous studies incorporating dynamic resistance exercise training in conjunction with pharmacotherapy have also achieved favorable improvements to glycemic control in middle-aged and elderly NIDDM populations.[9, 21, 22] Following 16 weeks of triweekly progressive resistance exercise (30-80% 1 RM), both Bacchi et al. [21] and Cauza et al.[22] obtained significant reductions to fasting blood glucose, HbA1c and insulin resistance. Contrary to the use of a control group, both compared data subjects to a secondary cohort of aerobic training subjects. However, it is noteworthy that subjects who underwent aerobic exercise training experienced a greater attenuation to fasting blood glucose (-15.2 vs -12.0 mg/dL) additive with a two-fold increase in glucose disposal rate (1.15 vs. .52 mg/kg FFM^{-1}/min).[21] Additionally, Cauza et al.[22] reported that subjects undergoing resistance training not only significantly improved fasting blood glucose but also observed attenuated plasma insulin concentrations, as well as improved insulin sensitivity. However, it was also noteworthy that resistance exercise training subjects performed 3-6 sets of 10-15 repetitions verses 1-3 sets of 8-10 repetitions and depicted elevated fasting blood glucose values at baseline compared to aerobic training counterparts.[22] While both employed the use of 9 resistance exercises targeting similar muscle groups, Casteneda et al.[9] only observed significant reductions to HbA1c (12%) with no change to fasting blood glucose. Also, changes in insulin resistance were unknown as it was not a measured parameter. Although Castaneda and colleagues only employed the use of 5 resistance exercises with fewer repetitions, the quantity or dosage of medications must be considered when observing a lack of change to fasting blood glucose. [9] Moreover, Casteneda and colleagues employed a control group, which depicted a lack of improvement to glycemic control in the absence of exercise.

Interestingly, both Casteneda et al.[9] and Bacchi et al.[21] focused their interests specifically to Hispanics afflicted with NIDDM, while the ethnicity group studied by Cauza and colleagues remains unclear. Although results of each protocol were inconclusive, it can be further determined that resistance exercise training is an effective and safe modality of supplemental treatment secondary to anti-hyperglycemic medication. More importantly, Cauza et al.[22] reported a 12% reduction in sulphonylureas while Bacchi et al.[21] and Casteneda et al.[9] also reported dosage reductions or discontinuance of anti-hyperglycemic medications.

Resistance Exercise in Non-Diabetic Populations

The American College of Sports Medicine recommends a minimal of 2-3 days of weekly resistance exercise for a multitude of populations.[35] Miller et al.[11] assessed the efficacy of high intensity resistance exercise on glucose tolerance. Similarly, Rice et al.[15] proposed improvements to BGT following resistance and aerobic exercise additive with a daily caloric restriction of 1,000 kcals. While both studies utilized healthy males, Miller and colleagues yielded a 7% reduction in BGT, whereas Rice et al.[15] obtained a similar "within group" difference within the resistance training group, only.

Although both studies used similar training frequencies, exercising muscle groups, the administration of pre and post oral glucose tolerance tests, and training intensities, several differences were observed. While Miller et al.[11] recruited 8 healthy college-aged men with no control or follow-up period, Rice et al.[15] enrolled 33 obese middle-aged males and incorporated a separate aerobic training and control group. Additionally, the subjects recruited by Rice and colleagues seemed to have had impaired BGT, which may have further corresponded to the degree of glycemic improvements. Furthermore, Miller at al.[11] administered a 150-minute OGTT with a bolus dose of 100g, while Rice et al.[15] administered a 300-minute OGTT with bolus dose of 75g. As a result, the inconsistencies between glucose dosage and test duration may have provided results that were incomparable.

Isometric Exercise and Improved Health Parameters

Isometric exercise training (IET) is a resistance exercise modality that have been shown to elicit significant improvements to health parameters such as, reductions to resting blood pressure.[24, 25, 32] A recent meta-analysis projected IET as the most effective modality for reducing resting blood pressure when compared to dynamic resistance and aerobic training.[32] After 8 weeks of isometric handgrip training, both Millar et al.[34] and Taylor et al.[33] observed significant reductions in resting blood pressure in middle-aged hypertensive men and women. Although NIDDM and hypertension are differing conditions, both share common elements such as increased peripheral vascular resistance and vascular pressor responses in conjunction with decreased baroreceptor sensitivity and vascular compliance.[42, 46] As the risk of cardiovascular disease and premature mortality is heightened during the presence of hypertension and or diabetes, it may be desirable to implement IET as a common treatment modality to improve resting blood pressure while observing for any potential influence to glycemic parameters.[28, 42, 46]

Isometric Exercise Training and Blood Glucose Tolerance

Little is known regarding an association between an acute bout of IET and subsequent changes to BGT. Despite a lack of evidence, Dolkas and colleagues first observed if bilateral leg IET performed at 21% maximal voluntary contraction (MVC) would elicit improvements to BGT compared to sustained isotonic exercise or control conditions, while spending prolonged periods on bed rest and administered controlled diets.[27] While IET was administered as a novel approach to potentially influence glycemic parameters, significant improvements to BGT were only observed during a supine isotonic exercise bout at 68% $VO2_{max}$. Because the cohort also contained a small number of young healthy males (N = 7) without abnormalities of blood glucose homeostasis, the degree of potential improvements could have been very minimal.[27] While conducting insulin and glucose infusion, Peltoniemi and colleagues reported that 2-second unilateral isometric leg contractions performed at 10% MVC for 105 minutes significantly contributed improved glucose uptake in 11 healthy young males.[41] Although both studies implemented supine isometric leg exercise utilizing cohorts of young and healthy males, Peltoniemi et al.[41] recruited aerobically trained males whereas, Dolkas et al.[27] facilitated sedentary lifestyle behavior by implementing sustained bedrest periods while conducting isometric and isotonic exercise sessions. Most importantly, while Dolkas et al.[27] performed a baseline period verses a control group, Peltoniemi and colleagues used a secondary cohort of males afflicted with type I diabetes. Contrary to the healthy group of males, the diabetic cohort experienced a blunted response insulin and exercise mediated glucose uptake.[41] Because of the inconclusive results of the aforementioned studies, more work is required to determine if skeletal muscle glucose uptake may can be improved by isometric exercise under a hyperinsulemic state.[6, 41]

Suspected Mechanics of Improved Glycemic Control

Although the exact mechanism responsible for improved glycemic control following resistance exercise training has not been elucidated, many speculations regarding the physiological changes have emerged in the literature. It has been suggested that increased abdominal adiposity in conjunction with a sedentary lifestyle causes an increase in insulin resistance.[6] Interestingly, an increase in lean body mass with a subsequent reduction in adipose tissue has been demonstrated to improve glycemic parameters in obese populations.[7, 15] Ivy and colleagues proposed that augmented insulin concentrations following exercise can acutely dilate vessels, which may further contribute to a hyperemic response coupled with an increase in blood glucose extraction.[6] Additionally, it has been proposed that chronic hyper-insulinemia can influence skeletal muscle fiber type by triggering a transition to fast-oxidative fibers.[3] As a result, habitual exercise may then influence muscle fiber type further improving glycemic control, as oxidative fibers are believed to be more insulin sensitive.[3, 6] Additionally, it has been suspected that when muscles are electrically stimulated in the absence of insulin, GLUT4 translocation is activated due to an accumulation of calcium ions, AMPK and nitric oxide synthase. As a result, blood glucose clearance has been shown to increase despite an absence of insulin.[13, 26] Although the mechanisms of IET and improved glycemic control are unknown, additional research specific to abdominal adiposity, influences of skeletal muscle fiber, hyperemic responses, and exercise-stimulated glucose transport may be needed in order to reach a universal agreement regarding IET adaptations.

Summary

Although evidence demonstrates that dynamic resistance exercise is a safe and clinically effective modality of supplemental therapy, improvements to BGT within NIDDM populations have remained inconsistent. Because of the various methodology, training durations and intensities as well as differing muscle groups selected for exercise, there has yet to be a universal protocol for dynamic resistance or isometric exercise that is beneficial for diabetes management or prevention. Additionally, the dosage of glycemic loads that have been administered in recent studies have not been consistent with one another, which may or may not affect the response outcome. Although there are inconsistencies within the literature, recent studies have provided implication that dynamic resistance exercise performed triweekly at an intensity 30-80% 1 RM can significantly improve glycemic control. Moreover, studies have also indicated that dynamic resistance training is not an effective method of improving BGT. However, the utilization of IET and its effects on glycemic parameters is very sparse. As a result, future research incorporating dynamic resistance training and IET utilizing randomized control trials must be implemented. In doing so, this may provide important information regarding the effects of IET on glycemic control compared to dynamic resistance training. Additionally, future studies should specify more information regarding anti-hyperglycemic medications used such as drug class, dosages, and alterations to pharmacotherapy regimens within study cohorts. This will better allow future researchers to separate the potential effects of IET on glycemic control verses medications alone. Moreover, future studies should incorporate equal numbers of males and females in treatment and control groups as well as age and medication stratification. Overall, IET serves as a training modality that may have potential to not only improve resting blood pressure but glycemic kinetics as well. However, it is currently unknown if isometric exercise through programmed training or an acute bout may improve glucose uptake. As the purpose of our study is to observe if isometric exercise elicits an acute influence to BGT as it has shown to do with resting blood pressure, the implementation of isometric exercise may serve as a therapeutic approach for those afflicted with both NIDDM and hypertension.

CHAPTER 3: MATERIALS & METHODS

Sixteen males (N = 16) were successfully recruited and enrolled in this study. Participants were excluded if one's resting blood pressure > 160/100 mmHg, FBG > 180 mg/dl, active use of tobacco products (including smokeless) within the preceding 6 months, unable to read and understand English language, actively using prescribed cardiovascular medications, were not of male gender, actively engaged in physical activity > 90 minutes/week for the preceding 3 months, or had any physical limitations that would be exacerbated by isometric exercise.

Sampling Techniques and Recruitment

A scripted email was distributed to all male students of UNC Charlotte, which conveyed the nature and importance of the study. In hopes of further expanding the study's sample population, the research team communicated information regarding the study to males within the local community outside of UNC Charlotte. Each participant who expressed interest was screened by telephone comprising of a detailed explanation of the study followed by a short series of questions to determine eligibility. Each participant who expressed interest and was determined eligible was scheduled for an orientation session, which took place in the laboratory of systems physiology at UNC Charlotte.

Study Design and Methodology

This experimental investigation contained an applied approach. Each participant acted as their own control during the orientation session (Day 1) and transitioned to exercise treatment during the exercise session (Day 2). Sessions were separated by ≥ 24 hours. Each participant visited the laboratory twice. The independent variable (X) consisted of isometric exercise treatment, which was conducted at an intensity of 15%

maximal voluntary contraction (MVC). BGT served as the dependent variable (Y). While each participant attended both sessions, blood glucose was assessed at six different time points; 0 (fasting assessment) and then 30, 45, 60, 90, and 120 minutes following the consumption of a glucose beverage. However, during the exercise session, we took an additional blood glucose sample immediately following the completion of the exercise bout.

Orientation Session

All participants entered the laboratory fasted for 8 hours, during which time the consumption of water was only permitted. Additionally, participants abstained from consuming caffeine and or alcohol for 12-24 hours. Each participant was notified one week prior to their scheduled orientation session and instructed to arrive in a fasting metabolic state and to maintain their normal diet for 3 days prior to the session. Additionally, participants were notified to refrain from exercise or physical activity 48 hours prior to the session. Upon arrival, each participant completed a Pre-Activity Readiness Questionnaire (PAR-Q) in which they had to have answered, "Yes" to: “Have you abstained from exercise in the past 48 hours? Have you fasted from food for 8 hours? Have you abstained from alcohol and caffeine intake for the past 12-24 hours?” Furthermore, each participant must have reported that they had not experienced dizziness within 8 hours prior to the session. If the participant answered "No" to any of the following questions or stated that they have felt dizzy or lightheaded within the last 8 hours, the session was terminated and rescheduled. Each participant then underwent a resting blood pressure (American Diagnostics Corporation) assessment following 15 minutes of seated rest. Each participant was then administered an informed consent.

Completion of the PAR-Q as well as agreeing to the informed consent adhered to the compliance guidelines set by the 1964 Declaration of Helsinki. Each participant's FBG was then assessed (MHC Medical Products). If the participants FBG exceeded 180 mg/dl, the participant was excluded from the study and advised to seek consultation at a local healthcare clinic.

Oral Glucose Tolerance Test and Maximal Strength Assessment

Each participant consumed a Trutol 75 glucose beverage (Thermo Fisher Scientific, INC) which they were instructed to fully consume within three minutes. Blood glucose was then assessed at 30, 45, 60, 90, and 120 minutes following consumption. Once the glucose tolerance test was completed, maximal bilateral quadricep strength was then assessed using a isokinetic dynamometer (Biodex Medical Systems, INC). Each participant was properly fitted to the device and their seat settings were recorded. Utilizing maximal tension, participants were then instructed to push with both legs against an immovable arm fixed at a 90 degree angle for 10 seconds. The ten-second trial was repeated 3 times with 10 seconds of rest between each trial. Maximal torque production was observed by the primary investigator during all 3 attempts. A submaximal percentage of 15% was calculated from the highest attempt and served as the specific workload intensity for each participant during their exercise session. For familiarization purposes only, participants were permitted to complete a brief isometric contraction on the isokinetic dynamometer at 15% MVC.

Body Composition

Height and weight was first assessed using a wall-mounted stadiometer and a calibrated scale, which was linked with the BODPOD (Life Measurement Instruments). Participants were instructed to remove all jewelry, eyewear, and clothing for the exception of shorts or tight fitting undergarments. Participants were then provided an airtight swim cap to place over the scalp. Participants entered the enclosed chamber and remained motionless during the air displacement plethysmography test.

Exercise Session

For each exercise session, participants were instructed to follow the same fasting criteria as did for the orientation session. Each participant was asked 5 questions regarding their fasting metabolic state (identical to the orientation session) followed by a FBG assessment. Participants were next seated on the isokinetic dynamometer and adjusted to their specific seat settings. Once seated and secured, the participants then consumed a dextrose 75g beverage within a 3-minute duration. Immediately following the ingestion of the beverage, the investigators initiated a stopwatch and the exercise protocol began. 2-minute contractions were performed 6 times at 15% MVC. Each 2-minute contraction was separated by one minute of rest. Rate of perceived exertion (RPE) immediately assessed following each 2-minute contraction. Once the exercise protocol was completed, an immediate blood glucose assessment was taken. Participants were will then instructed to remain seated, as investigators assessed blood glucose at 30, 45, 60, 90 and 120 minutes following the beverage consumption.

Statistical Analysis

Rates of glucose clearance between sessions or between sexes was determined using a linear regression analysis. Evaluations in changes of serum glucose differences over time for both sessions were analyzed by a 2-way analysis of variance (ANOVA) with repeated measures. Statistical differences were only considered if the P value at measured time points was $< .05$. Tukey's post-hoc analysis was used for pairwise comparisons. Glucose tolerance was determined by calculating the area under the curve (AUC) for serum glucose over time. This analysis provided an effect size for each participant regarding the changes to blood glucose during both levels of treatment. A parametric T-Test was performed to assess differences in all fasting serum glucose samples between sessions. A second parametric T-Test was performed in order to assess the differences in FBG levels compared to levels taken immediately post-exercise. Finally, correlational analyses were used to assess the relationship between lean body mass and glucose clearance.

CHAPTER 4: RESULTS

Pilot Data and It's Influence of Isometric Exercise on Glucose Tolerance

Pilot data represents differences in BGT over time between males and females proceeding the completion of 6, 2-minute bilateral isometric leg contractions at 15% MVC. These changes can be observed in **Figure 1A**. The rate of glucose disposal between male and female cohorts was assessed from a linear regression model, which further compared the slope differences from time point 45 minutes post-consumption to 120 minutes post consumption thus detecting any significant changes between the two slopes. Interestingly, our findings indicate a significantly steeper slope in male participants (N = 6; p = 0.03) compared to female participants (N = 7). This finding indicates that the rate of glucose disposal within the male cohort may have been accelerated following the exercise protocol when compared to the female cohort. These results can be observed in **Figure 1B**.

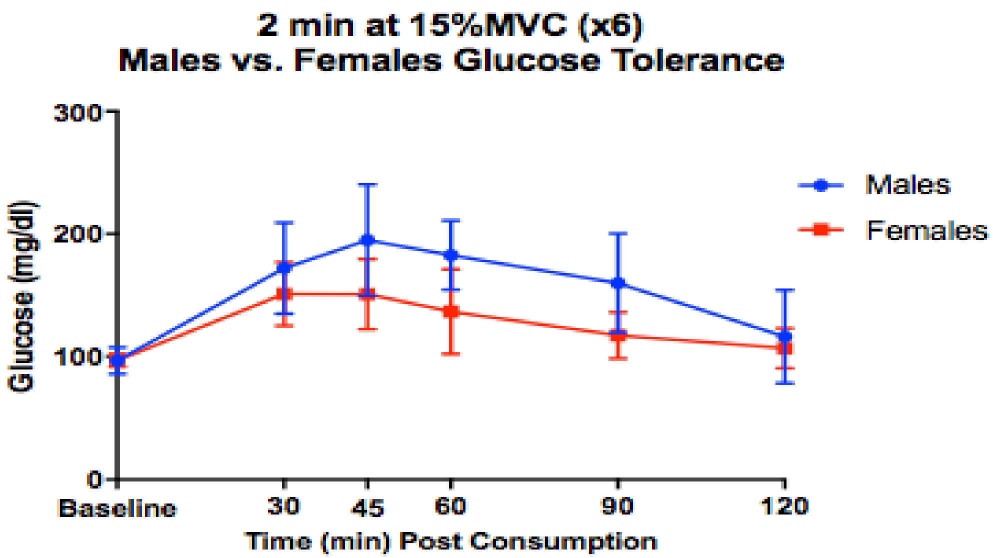

Figure 1A: Overall differences in in blood glucose tolerance following one session of isometric exercise utilizing bilateral quadriceps

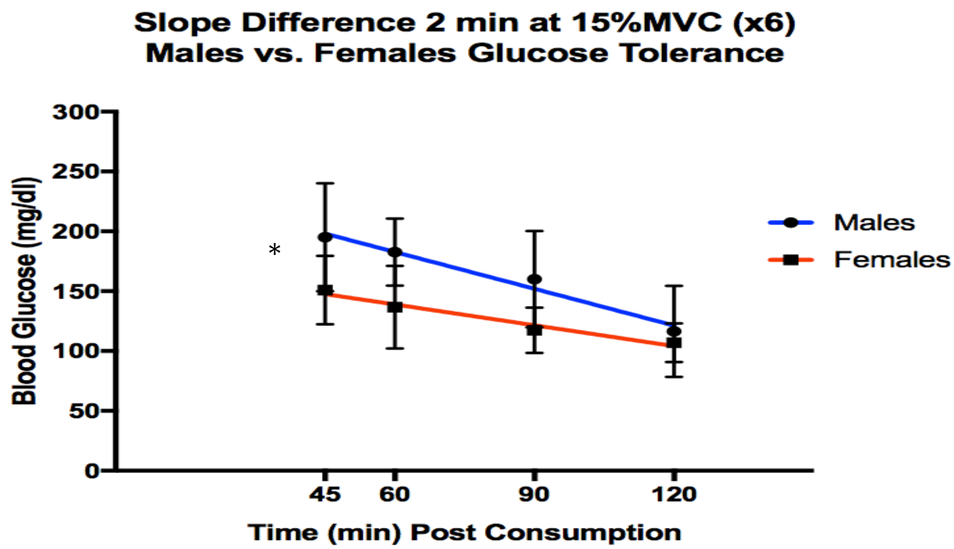

Figure 1B: Slope differences between males and females following one session of isometric exercise (P < .05)
** indicates significance P < .05*

Males Blood Glucose Tolerance

There were no significant differences in FBG samples prior to the administration of an OGTT during the orientation and exercise sessions (p = 0.33). Our study contained 100% adherence with no dropout or concerns with non-compliance. Demographic data for the study's 16 male participants can be observed in **Table 1**. There was no significant interaction effect regarding isometric exercise influencing BGT at any specific time point (p = 0.24; Figure 2A). Moreover, there was an overall variance of 47.8% regarding blood glucose responses following the administration of an OGTT and isometric exercise. Our results also elicited that the consumption of an OGTT preceding a brief exercise protocol resulted in significantly higher serum glucose immediately post-exercise compared to pre-exercise fasting levels (p = 0.01; Figure 2B). In order to assess the rate of glucose disposal in each participant and if isometric exercise influenced the disposal rate, area under the curve (AUC) was calculated for each orientation and exercise session. There was no significant difference between sessions; further suggesting that isometric exercise did not influence the rate of glucose disposal (Figure 2C).

Participants	N = 16
Age (Yrs.)	24 ± 3
BMI	26 ± 5.16
Resting SBP (mmHg)	113 ± 8
Resting DBP (mmHg)	72 ± 5
FBG (mg/dl)	104 ± 8.8
LBM (Kg)	63.6 ± 12.6
Fat Mass (Kg)	21.9 ± 14.9
RPE	17 ± 1.88
MVC (Newtons)	312.75 ± 61.2
15% MVC (Newtons)	46.6 ± 9.2

Table 1: Study participant including body composition, rating of perceived exertion following exercise, maximal strength capacity for bilateral quadriceps and allotted exercise intensity. All values are represented as a mean with a standard deviation (±).

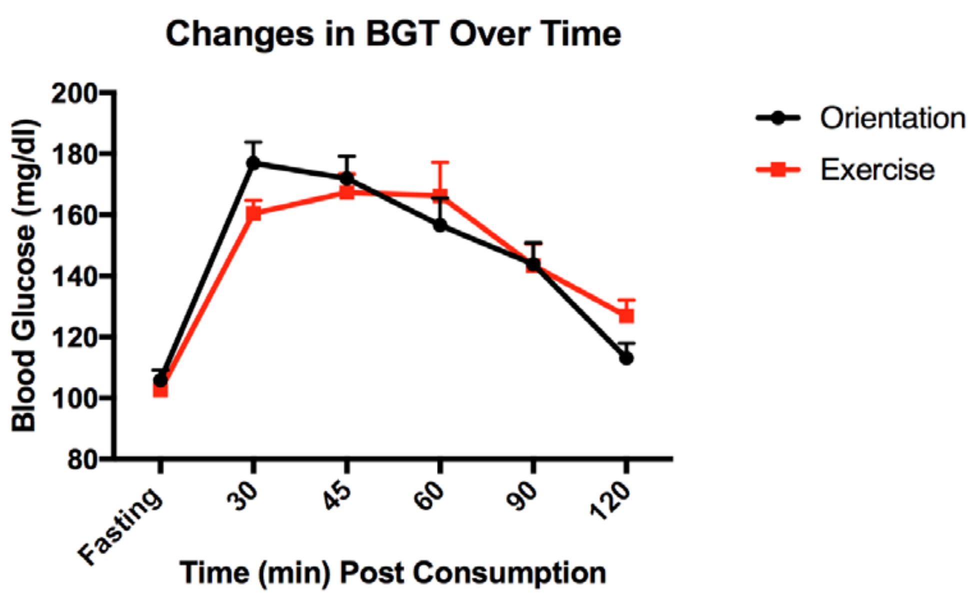

Figure 2A: Changes in BGT over time for both exercise and orientation session (P > .05)

Figure 2B: Differences in serum glucose samples pre and post exercise (P < .05)
** indicates significance P < .05*

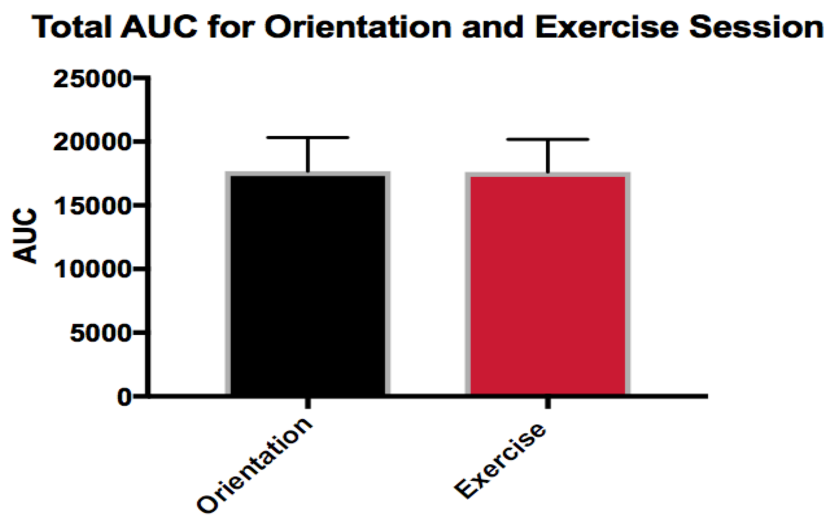

Figure 2C: Differences in Area Under Curve between orientation and exercise session (P > .05)

In order to assess a relationship between lean body mass (LBM) and glucose clearance capacities, **Figure 2D** demonstrates the duration of hyperglycemic exposure relative to the quantity of LBM for each participant. Our results indicated no linear relationship between LBM and AUC for glucose tolerance (r = - 0.18; p = 0.48).

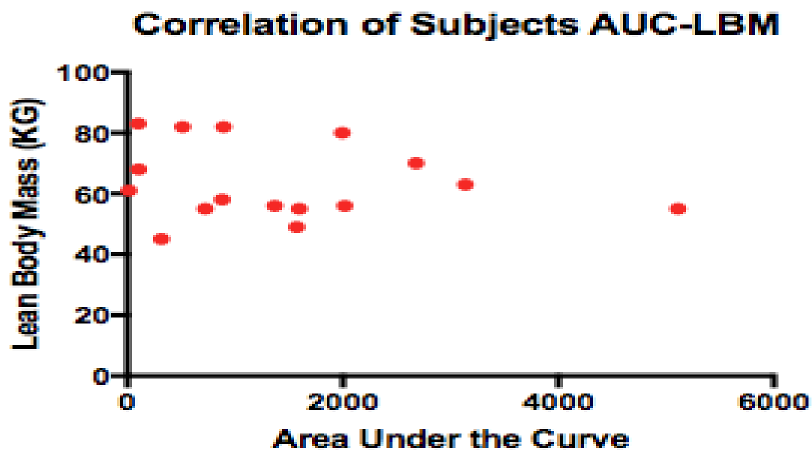

Figure 2D: Correlational analysis between LBM and AUC for glucose tolerance following 6, 2-min contractions at 15% MVC.
($P > 0.05$; R square = 0.0324).

Pilot and Present Data Combined

While considering the significant difference in slopes between males and females from our pilot data, we collaborated all data for further analysis. Changes in BGT over time following the administration of an OGTT and exercise for all males can be demonstrated in **Figure 3A**. When comparing the orientation and exercise session, there was no significant interaction effect regarding changes in BGT at any specific time point (p = 0.48). Our analysis simply indicated that time accounted for 47.76% of total variance, while blood glucose alone and the interaction effect accounted for .14% and .90% of total variance. In consideration of the foregoing, our analysis confirmed that there is a 49% chance of randomly observing a significant interaction effect regarding changes in BGT following isometric exercise during any specific time point with a cohort of this size (N = 22). Furthermore, it was of interest to determine if the isometric exercise further contributed to an accelerated rate of glucose disposal. **Figure 3B** portrays that there was no significant change to the rate of glucose disposal following one bout of isometric exercise when compared to the orientation session (p = 0.83). This finding contradicts our pilot data regarding the rate of glucose disposal between males and females following isometric exercise. Finally, the rate of glucose disposal between all males and females was determined by a linear regression model and can be observed in **Figure 3C**. These results further indicate that one bout of isometric exercise did not significantly influence glucose disposal rates between 22 males and 7 females (p = 0.29).

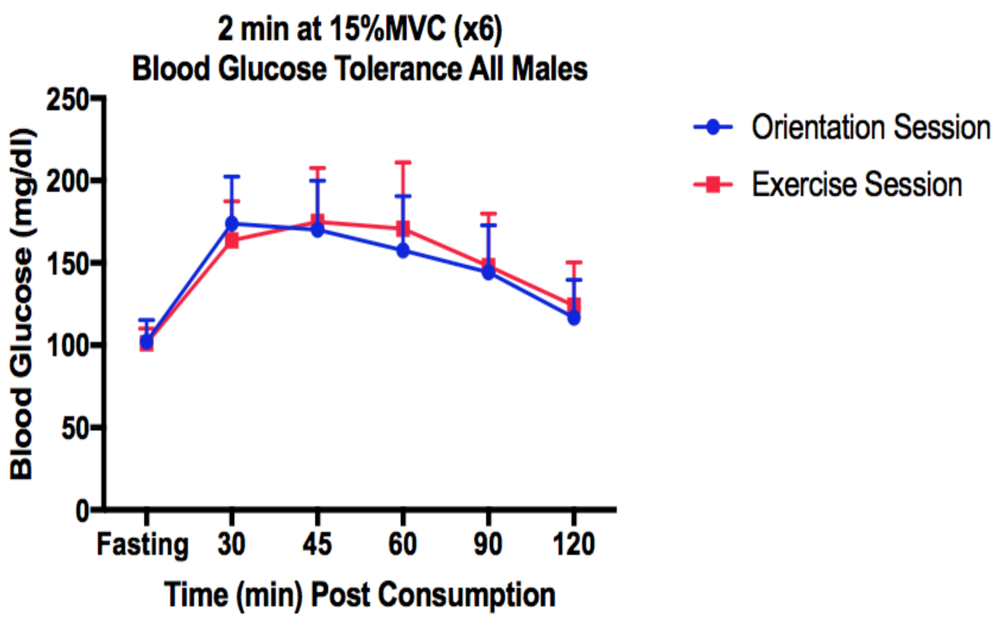

Figure 3A: Changes in BGT over time for all males (including pilot data) during both orientation and exercise sessions (p > 0.05)

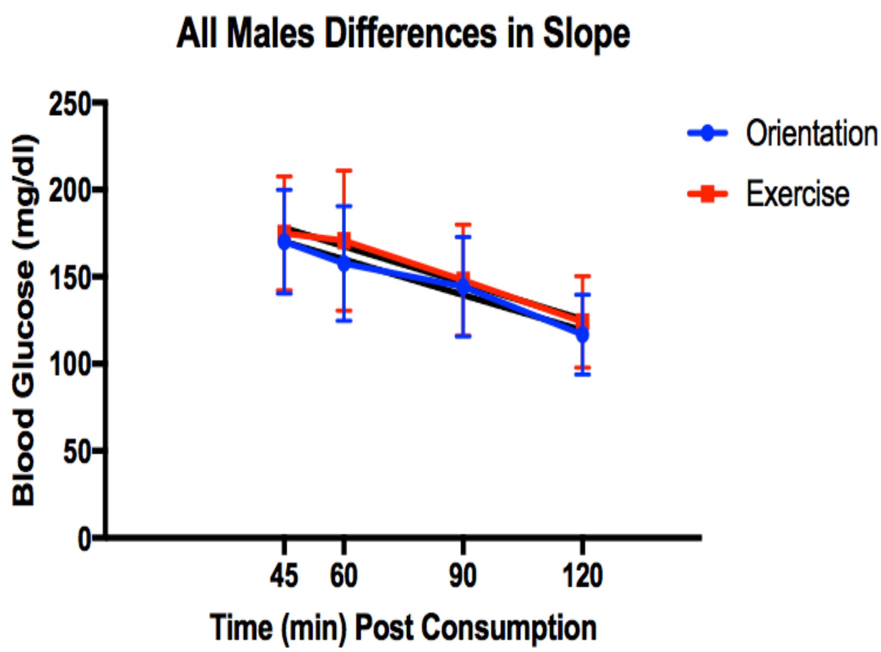

Figure 3B: Overall slope differences for both orientation and exercise sessions ($p > 0.05$). Data includes all males from current study and pilot work.

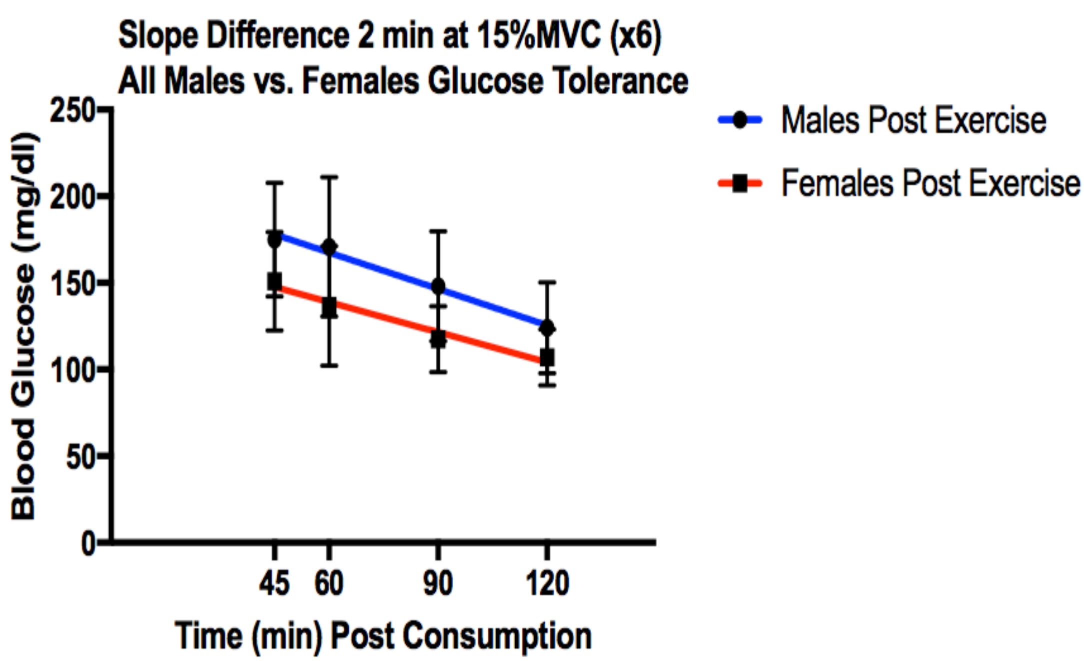

Figure 3C: Overall difference in slope between males and females following isometric exercise ($p > 0.05$).

CHAPTER 5: DISCUSSION

Considering our pilot data, it was depicted that BGT within a small group of males (N = 6) returned to pre-exercise fasting levels significantly faster than their female counterparts following the administration of an OGTT and completion of 6, 2-minute isometric bilateral contractions of both quadriceps. In order to gain further clarity regarding this response, the overall focus of our study was to observe if this desirable influence could be further elicited in a larger sample size of males with similar lifestyle characteristics. Our results indicated that 6, 2-minute isometric contractions at 15% MVC had no significant interaction on BGT at any assessment time point during the OGTT. Additionally, glucose clearance rates were not different between sessions, further suggesting that isometric exercise did not influence skeletal muscle glucose uptake. The consumption of the glucose beverage followed by the completion of the exercise resulted in a duration of 20 minutes. Serum glucose was significantly higher following the cessation of exercise compared to fasting levels, which may be due glycogenolysis as a result of sympathoadrenal hyperactivity additive with hyperglycemia due to the OGTT. Furthermore, the absence of a significant linear relationship between LBM and glucose disposal rates may suggest that surface area of LBM composes only a partial role in glucose disposal, in addition to plasma catecholamines, and neurotransmitters of the central nervous system.[39] When combining our study's data with our pilot work, the isometric exercise protocol did not significantly influence BGT between sessions at any specific time point during the OGTT. Interestingly, there were also no significant differences in slope of responses between sessions or sexes.

The lack of significant change to BGT suggests that this specific glycemic parameter is not always susceptible to change following both acute and programmed resistance exercise, in which our results further agree with a great deal of prior literature.[9, 11, 12, 14, 15, 22] Although significant improvements to long-term parameters such as, HbA1c and insulin sensitivity have been observed proceeding the completion of programmed dynamic resistance training, numerous studies have also demonstrated significant changes to BGT.[15, 16, 21, 22, 31] Notably, Ivy and colleagues reported that exercise induced changes to BGT are more likely to be observed in elderly individuals than younger individuals, as the risk of impaired glucose tolerance and insulin resistance increases with aging.[6] Our results are in agreement with Dolkas et al.[27] as there were no significant changes to BGT following bilateral isometric leg exercise at a submaximal intensity. Our study only required participants to conduct one session of isometric exercise at 15% MVC as opposed to bi-daily sessions for 2 weeks at an intensity of 21% MVC. Dolkas and colleagues speculated that significant improvements to BGT and insulin sensitivity as a result of IET, would require 3 hours of daily isometric exercise in order to equate to the metabolic demands of an isotonic exercise performed at 68% VO2 max.[27] After performing 4 sets of 6-8 repetitions performed at 85% 1 RM, Black et al.[45] observed the most significant improvements to FBG and insulin resistance in subjects afflicted with impaired fasting glucose. The authors further speculated that high intensity resistance exercise significantly influences insulin sensitivity while higher volume may influence BGT.[45] Additionally, one bout of progressive resistance exercise resulted in significant improvements to insulin sensitivity, while BGT did not change in subjects afflicted with NIDDM.[20] As a result, Flukey and colleagues concluded that resistance exercise may further improve insulin sensitivity without effecting BGT.[20]

Our participants reported a mean RPE value of 17 $\pm$1.88 (very hard) during the brief exercise session. As a result, the exercise intensity may have been high for our sedentary participants thus leading to sympathoadrenal hyperactivity. Although it has been reported that plasma catacholamines remain elevated following a strenuous bout of aerobic exercise, it is unclear whether this occurrence may also proceed a strenuous bout of resistance exercise.[46] Interestingly, exercise training can significantly influence hexokinase II enzyme activity further eliciting accelerated rates of serum glucose clearance.[6, 44] Due to the sedentary lifestyle of our participants, glycogen storage capacity and enzyme activity responsible for glucose phosphorylation, oxidation and storage such as hexokinase II, may have impacted skeletal muscle glucose uptake.

Though the specific mechanisms for improved glycemic parameters following exercise have not been elucidated, it has been suggested that the rate of blood glucose disposal may be associated with surface area of LBM and the degree of insulin sensitivity.[2, 7, 15] Although we did not measure insulin sensitivity, our results indicate that blood glucose clearance capacities may have been independent of LBM. Moreover, recent literature has suggested that the action of insulin may be hampered due to an accumulations of free fatty acids competing for substrate use, as well as extra-myocellular fat located within the muscle further obstructing glucose uptake.[6, 41, 43]

As the mean BMI for our participants was categorized as "overweight," insulin resistance due free fatty acid accumulation, high volumes of refined sugar intake, as well as overproduction of tumor necrosis factor-α must be considered.[6, 43] Ivy and colleagues proposed that post-exercise hyperemia additive with the presence of insulin may lead to acute vasodilation, thus contributing to improved glucose extraction.[6] Because isometric contractions result in partial arterial occlusions, it seems reasonable to agree with this proposal. However, we did not measure the degree of peripheral vascular resistance nor did we observe any significant changes to BGT.

The limitations of both our study and pilot data first include that of a small sample size of males (N = 22) ages 18-45 years. Additionally, our only glycemic parameter assessed was FBG, whereas numerous studies have included the assessment of insulin resistance and HbA1c.[9, 11, 12, 15, 38] Body composition assessments were measured by air displacement plethysmography, which has a ±2.0 to ±3.7% standard error of measure.[42] Additionally, there was seemingly an extensive variation in body composition, which may have influenced the rate of glucose clearance potentially due to insulin resistance.[43] Furthermore, our correlation analysis for LBM and AUC did not include the male participants of our pilot work, as LBM data was not available. Finally, our study did not contain a follow-up period as recent investigations have obtained significant outcomes to HbA1c, BGT and insulin resistance following 12-24 hours of exercise training or one bout.[17, 18 20, 44, 45, 46]

Although our findings did not indicate any significance, our study contributes to the limited literature regarding the acute effects isometric exercise and serum glucose tolerance. As very few studies have investigated this potentially influential relationship, much additional research is needed. Randomized control trials utilizing large cohorts of participants afflicted with NIDDM or impaired glucose tolerance are needed in order to truly validate the impact of isometric exercise on BGT, as individuals with abnormal glycemic parameters contain a higher susceptibility for change.[14, 35] As it has been speculated that exercise intensity and volume may influence insulin sensitivity and BGT, IET programs containing various workloads may be of importance.[45] Additionally, it may be beneficial to incorporate control and placebo treatment groups rather than treatment groups alone. As a great deal of literature projects changes to HbA1c and insulin sensitivity following long term programmed resistance training, the assessment of these variables in conjunction with serum glucose tolerance may provide a comprehensive overview regarding the long term effects of IET. [12, 14, 15, 22] Moreover, assessing changes to muscle fiber type isoforms throughout an IET program may be of importance as different muscle fibers contain differing oxidative and glycolytic capacities, which are susceptible to change with exercise training.[2, 6] Lastly, follow-up periods proceeding the completion of IET programs are needed in order to confirm if any potential training-induced benefits to glycemic parameters may sustain or diminish.

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