5-2022

Postprandial Hemodynamics in Hispanics with and Without a Family History of Type 2 Diabetes

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POSTPRANDIAL HEMODYNAMICS IN HISPANICS WITH AND WITHOUT A FAMILY HISTORY OF TYPE 2 DIABETES.

A Thesis

by

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Submitted in Partial Fulfillment of the

Requirements for the Degree of

MASTER OF SCIENCE

Major Subject: Exercise Science

The University of Texas Rio Grande Valley

May 2022

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May 2022

ABSTRACT

Figueroa, Gabriel A., Postprandial Hemodynamics in Hispanics with and without a Family History of Type 2 Diabetes. Master of Science (MS), May, 2022; 70 pp., 1 table, 11 figures, references, 108 titles.

Hispanics of the Rio Grande Valley (RGV) have the highest rates of obesity and type 2 diabetes (T2D) in the country, conditions often associated with cardiovascular disease and increased mortality. This study investigated the physiological factors affecting postprandial hemodynamic responses differently between FH+ and FH- groups. Thirty-one healthy Hispanic individuals volunteered in this study. Overall, FH+ individuals had higher pressures at rest compared to FH-, However, these differences were not statistically significant. When controlling for blood chemistries such as blood glucose, cholesterol, lipoproteins, and triglycerides, family history appears to have no effect on fasted or postprandial hemodynamics and pulse wave reflection.

DEDICATION

I dedicate this thesis project to God Almighty, creator of Heaven and Earth, my cornerstone, my deliverer, and source of wisdom, understanding, and inspiration. Through trial and tribulation, He has lifted me on high and delivered me from peril and failure. I dedicate this project to my family, Belisario, Maria Elena, Obed, and Cesar, who have supported me unconditionally. To my wife and son, who have motivated me to finish what I have started. To my friends David, Crystal, Eddie, Louie, Pete, Tiffany, Dr. Zundell, and Braady who have all taken the time to listen, encourage, and mentor me. To my pastors, Fernando and Enereida Salazar, thank you for praying for me. I love you all. God bless you.

ACKNOWLEDGMENTS

Thank you to Dr. Samuel Buchanan for always being there to counsel me. Without your guidance, patient, and words of encouragement, I would have been lost. Thank you to Dr. Yu Lun Tai and Dr. Ryan D. Russell for laying the groundwork of this project. To Dr. Samuel Buchanan, I owe you a large debt for takin the time to nurture me, guide me, and listen to all my questions and ideas. Without you, Dr. Buchanan, I would be hopelessly lost. My thanks go to all the volunteers who participated in this research project and to Jaime Rodriguez, Alexandro Rodriguez, Smaran Marupudi, and Javier Ybarra for assisting with data collection.

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CHAPTER I

INTRODUCTION

34.2 million people living in the United States, alongside another 88 million, are diagnosed with diabetes and prediabetes, respectively (CDC, 2020). The American Heart Association has previously indicated that the diagnosis of Type 2 Diabetes (T2D) doubles the risk of developing and dying from cardiovascular disease (Jeannette & Wick, 2021). The main drivers of the T2D epidemic include overnutrition and increased sedentary behavior (Fletcher et al. 2018). Chronic overnutrition and sedentary behavior are obesogenic promoters that can induce metabolic disease. The relationship between obesogenic factors and metabolic disease is dynamic, such that increases in fat mass gives rise to glucose intolerance, insulin resistance, hypertension, arterial stiffness, and hepatic steatosis. Collectively, these comorbidities are known as metabolic syndrome. When left unchecked, insulin signaling and sensitivity is disrupted, which negatively impacts metabolism-related downstream signaling. When insulin signaling is impaired, a greater amount of insulin is needed to generate the proper response in tissues with insulin receptors. In essence, impaired insulin signaling, and chronic hyperglycemia-hyperinsulinemia are hallmarks of metabolic disease, such as T2D.

Many studies have aimed heavily on discovering the interplay between glucose-fatty acid (G-FA) metabolism, insulin's involvement in G-FA metabolism, and how insulin disruption leads to metabolic disease. Such studies have revealed the importance of skeletal muscle (Vincent et al. 2004; Vincent et al. 2005). Skeletal muscle's contractile actions impose a great metabolic demand (Baker et al. 2010). This increased metabolic demand is met by alterations in blood flow, facilitating nutrient, gas, and metabolic byproduct exchange between the vasculature and tissue. Naturally, skeletal muscle serves as the primary driver of whole-body glycemic control. In a post-prandial state, skeletal muscle is responsible for nearly 80% of insulin-mediated glucose disposal (Keske et al. 2017; Merz & Thurmond 2020). One important highlight is that glucose cannot freely enter myocytes. Glucose enters myocytes via facilitated diffusion with the help of glucose transporter 4 (GLUT4) translocation from the sarcoplasm to the sarcolemma. However, GLUT4 translocation does not occur without insulin downstream signaling. Insulin serves two dynamic roles in the delivery of glucose to the skeletal muscle. Firstly, insulin binds to receptors along the myocyte membrane. This binding triggers GLUT4 translocation to the sarcolemma, as previously mentioned. Secondly, and often underappreciated, insulin influences the release of nitric oxide (a strong vasodilator) from vascular endothelium, thereby increasing perfusion to the skeletal muscle.

In essence, when glucose levels rise in the blood (for example, after a meal), insulin is secreted by the pancreas to help mediate glucose entry into the myocytes, hepatocytes, and adipocytes. As previously mentioned, insulin dilates pre-capillary arterioles, allowing greater blood flow. Theoretically, increasing blood flow to insulin-sensitive tissues could result in greater glucose disposal. However, research has shown that increases in total blood flow to the skeletal muscle (or total limb flow) does not always signify improved nutrient exchange by the myocytes (Barret & Rattigan, 2012; Vincent et al. 2005). This suggests that there is an added level of complexity to

glucose disposal in skeletal muscle. Enter: the microvasculature. The microvasculature consists of pre-capillary arterioles and capillaries that modulate blood flow and control nutrient exchange. It is at the microvascular level that the actions of insulin greatly determine glucose disposal to maintain glycemic control. The loss of insulin sensitivity by the microvasculature greatly impairs insulin-mediated glucose disposal and vasodilation. Hyperinsulinemia, as a result of insulin resistance, disturbs vasomotor equilibrium in human skeletal muscle. This favors vasoconstrictive pathways which compromises arterial and arteriolar vasodilatory actions.

While T2D is a treatable disease, the risk for cardiovascular disease (CVD) and death due to CVD are high even when controlling for glucose levels, sedentary behavior, smoking, abnormal blood lipids, and hypertension (Jeannette & Wick, 2021). These findings suggest that people with T2D should be treated for CVD as early as possible. Interestingly, CVD and T2D share common ground in relation to pathophysiological factors. Risk factors for CVD include dyslipidemia, hypertension, inflammation, insulin resistance, oxidative stress, and obesity, all of which also raise the risk of developing T2D. These risk factors are associated with endothelial dysfunction, promoting endothelial remodeling, arterial stiffness, progressive vascular damage, atherosclerosis, and atherogenesis. Albeit, while both CVD and T2D stem from common ground, they are both complex disease with common and uncommon risk factors. However, it is not just individuals diagnosed with T2D who have CVD. For some time, it has been known that T2D gives rise to CVD. It is now evident that CVD risk precedes T2D. Those diagnosed with pre-diabetes and insulin resistance also show signs of long-term cardiovascular complications related to T2D (Brannick & Dagogo, 2018).

Abnormal macrovascular function is well established in individuals who are diagnosed with type 2 diabetes. This warrants the question; How soon can abnormal cardiovascular function be

detected in those at risk for both CVD and T2D? Intriguingly, preclinical manifestations of macrovascular and metabolic diseases such as vascular insulin resistance, arterial stiffness, and metabolic inflexibility precedes the onset of type 2 diabetes (Barret & Rattigan, 2012; Caballero et al. 1999; Giannattasio et al. 2008; Meijer et al. 2012; Nitenberg et al. 1993; Premilovac et al. 2014; Rahman et al. 2008; Rahman et al. 2009; Rahman et al. 2017; Russell et al. 2021; Stehouwer, 2018; Williams et al. 1996). Such abnormal macrovascular function is observed in healthy normotensive, normoglycemic offspring of parents with T2D (Caballero et al. 1999; Hopkins et al. 1996; Rahman et al. 2008; Rahman et al. 2009; Russell et al. 2013, Russell et al. 2021; Solanki et al. 2018; Warram et al. 1990; Xiang et al. 2008). In response to a simulated meal (mixed composition drink), research has shown that microvascular blood flow, brachial artery diameter and flow all increased in healthy individuals with no family history of T2D (FH-). However, these changes were absent in healthy offspring of type 2 diabetics (FH+) (Russell et al. 2021).

Hispanics are the largest minority group in the United States and have greater diabetes prevalence in both adults and children (Aguayo-Mazzucato et al. 2019). The Rio Grande Valley (RGV) region of South Texas made up of four counties, Starr, Hidalgo, Willacy, and Cameron County. It is home to a dense population of individuals riddled with cardiometabolic disease. Generally, T2D incidence is higher in Hispanics (National Diabetes Statistics Report, 2020). The prevalence of type 2 diabetes in the Rio Grande Valley has been reported to be 34.5%, tripling the national average (Meadows et al, 2018). The incidence of individuals being reported as overweight and obese in the Valley population are about 32% and 47.4%, respectively (Alaniz, 2018). Death due to CVD in the RGV has been reported to be 33% (CDC, 2020). As previously mentioned, the risk of CVD exists in otherwise healthy individuals who are offspring of parents with T2D. The

investigation of whether healthy Hispanic offspring of parents with T2D exhibit early cardiovascular dysfunction is warranted.

Purpose

While type 2 diabetics and prediabetics exhibit cardiovascular dysfunction, is not known whether any discrepancies exist between Hispanics from the RGV with a family history of T2D. Taking into consideration that the population of interest reside in an obesogenic and diabetogenic environment the purpose of this study is to 1) examine hemodynamics at rest and after administration of a mixed meal challenge and 2) determine whether a family history of T2D impacts cardiovascular function in otherwise healthy Hispanics.

Significance of the Study

The Rio Grande Valley region of South Texas is home to a high volume of Hispanics with first degree relatives with Type 2 Diabetes. Altered hemodynamics and arterial compliance in response to an oral glucose tolerance test (OGC) and mixed meal challenge (MMC) has been evaluated in Caucasian offspring of Type 2 Diabetics (Russell et al, 2013; Russell et al, 2021). However, the work by Russell et al, 2013 has shown that the use of an OGC impairs acute vascular function in healthy individuals, regardless of family history. An MMC has significantly less glucose and is sensitive enough to induce divergent responses across groups. Taking into consideration that the population of interest reside in an obesogenic and diabetogenic environment, this study would provide insight on the cardiovascular health of college-aged Hispanics residing in the Rio Grande Valley. Specifically, this study will investigate whether having a family history of T2D impacts central and peripheral hemodynamics at rest and postprandially.

Assumptions

1. The equipment used will be dependable and provide accurate information for each testing session.
2. All participants would complete the study in a timely manner.
3. Participants provided accurate information on health questionnaire and food logs.
4. All equipment used provided accurate results following calibration.
5. All participants arrived 10 hours fasted, hydrated, and rested on testing days.
6. All participants would complete the study.

Limitations

1. The study might not be representative of the population due to all participants being volunteers.
2. Health history, medical information, and diet will be gathered through self-report.
3. Participants will be asked to refrain from ingesting caffeine, alcohol, or engaging in intense exercise for at least 48 hours before testing, but activity will not be monitored.
4. Health history and medical information will be obtained through self-report.

Delimitations

1. Individuals with type 2 diabetes, BMI above 30, and/or cardiovascular disease were excluded.
2. Health history and medical information will be assessed before participation.
3. Individuals younger than 18 and older than 60 were excluded from this study.

Research Questions

1. Will there be significant divergent responses between individuals with and without a family history of T2D at rest?
2. Will there be significant divergent responses between individuals with and without a family history of T2D after MMC ingestion?

Hypothesis

1. The FH+ group will show increased pulse wave reflection compared to FH-.
2. The FH+ group will display higher hemodynamic pressures.

Operational Definitions

To aid the reader, the following terms are defined as used in this study:

1. **OGC/OGTT:** Oral Glucose Challenge/Oral Glucose Tolerance Test is a lab test to check how quickly an individuals' cardiometabolic system disposes of glucose from the blood into tissues metabolically active areas such as the skeletal muscle. The test is often used to diagnose diabetes.
2. **MMC:** Mixed Meal Challenge is a test to check how much insulin an individual produces after drinking the liquid meal beverage that contains fats, protein, and carbohydrates. The MMC in this study was comprised of 35g of protein, 5g of fat, and 30g of carbohydrates.
3. **PWA:** Noninvasive assessment technique that measures peripheral blood pressure waveforms and generation of the ensuing central waveform. Using data from the previous waveforms, augmentation index and central pressure can be attained.
4. **PWV:** Pulse Wave Velocity is a noninvasive assessment of the rate at which pressure waves travel down a vessel.

5. **AIx:** Augmentation Index assesses wave reflection and arterial stiffness and calculated as a ratio. This ratio is derived from the central pulse pressure and reflected pulse pressure.
6. **Hemodynamics:** Noninvasive analysis of the pulsatile driving pressures induced by the heart, flow characteristics of blood, and mechanical properties of the vessels.
7. **FH+:** Individuals with a first degree relative diagnosed with T2D.
8. **FH-:** Individuals with no family history of T2D for 2 generations.
9. **bSBP:** Brachial Systolic Blood Pressure
10. **bDBP:** Brachial Diastolic Blood Pressure
11. **bMAP:** Brachial Mean Arterial Pressure
12. **bPP:** Brachial Pulse Pressure
13. **HR:** Heart Rate
14. **cSBP:** Central Systolic Blood Pressure
15. **cDBP**: Central Diastolic Blood Pressure
16. **cPP:** Central Pulse Pressure
17. **AIx:** Augmentation Index
18. **AIx@75:** Augmentation Index adjusted for normal heart rate
19. **AP:** Augmentation Pressure
20. **RM:** Reflection Magnitude
21. **ED:** Ejection Duration
22. **BaDia:** Brachial Artery Diameter

CHAPTER II

REVIEW OF LITERATURE

Purpose

While type 2 diabetics and prediabetics exhibit cardiovascular dysfunction, is not known whether any discrepancies exist between Hispanics from the RGV with a family history of T2D. Taking into consideration that the population of interest reside in an obesogenic and diabetogenic environment the purpose of this study is to 1) examine hemodynamics at rest and after administration of a mixed meal challenge and 2) determine whether a family history of T2D impacts cardiovascular function in otherwise healthy Hispanics.

Pulse Wave Analysis & Arterial Compliance

Systemic arterial circulation is a vascular system of conduits that propels blood from the heart to the organs and tissues across the body. Pressures generated by left ventricular systole ejects blood with a sufficient force to create oscillatory arterial movement and forward blood flow. Due to the elastic capabilities of the arterial tree, arteries can preserve some of the systolic pressure created during contraction and maintain forward flow in the absence of ejected blood from the heart (diastole). While elasticity is a positive indicator of arterial health, arterial stiffness is highly associated with cardiovascular disease, heart failure, hypertension, strokes, coronary artery disease, atrial fibrillation, and myocardial infarctions (Bonarjee, 2018).

With each systolic action of the left ventricle, a pressure wave is created and travels through the entire vasculature. Vessels carrying blood bifurcates many times before arriving to its destined capillary beds. Therefore, when a pressure wave hits one of many resistance vessels (arterioles), a small reflection wave is produced. The summation of all these small reflection waves summates into one large, reflected pressure wave that travels back toward the heart. The time that the summated reflection wave takes to arrive at the heart is a typically utilized to assess arterial health. Specifically, stiff arteries show faster transit times whereas elastic arteries will have slower transit times. Chronically, arterial stiffness and fast reflection wave transit times is strongly correlated with left ventricular hypertrophy and hypertension due to increased afterload pressures that the left ventricle must pump against (Leutholtz & Ripol, 2019; Nichols et al. 2013). Many researchers have used applanation tonometry to assess aortic function and health. Several studies have utilized pulse wave analysis to measure pulse wave velocity and other measures of arterial stiffness. The consensus is that pulse wave analysis is a reproducible technique with accurate assessments of specific parameters related to arterial compliance (Doupis et al, 2016; Laugensen et al, 2016; Wilkinson et al, 1998).

T2D is associated with cardiovascular dysfunction and disease. Interestingly, macrovascular irregularities, such as arterial stiffness, precedes the onset of T2D by several years (Prenner & Chirinos, 2015). Urbina et al (2014) provided further evidence after investigating whether arterial stiffness is increased in otherwise healthy individuals with obesity or T2D compared with lean controls. This study reported that arterial stiffness is increased in healthy individuals in both the obese and T2D group even after correcting for known risk factors.

Acute Vascular Responses to Hyperglycemia

First degree relatives of individuals with T2D and hypertension are predisposed to previously mentioned conditions. Several studies have attempted to detect early vascular impairments in response to hyperglycemia. Vascular function and health can be noninvasively assessed by pulse wave analysis (PWA), which includes central and peripheral hemodynamics, cardiac output, and several indicators of arterial stiffness such as augmentation index. Solanki et al (2018) compared cardiovascular parameters using pulse wave analysis in healthy individuals with and without a family history of type 2 diabetes. 234 individuals participated in this study (FH+ = 117) (FH- = 117). FH+ individuals were shown to have higher brachial and central systolic and diastolic pressure as well as rate pressure product, pulse pressure, AIx@75, and pulse wave velocity compared to the control FH- group. Because of these parameters being significantly elevated in the FH+ group, this suggests that healthy FH+ have adverse cardiovascular profiles long before the onset of any metabolic disease such as type 2 diabetes.

Rahman et al. (2009) investigated arterial stiffness in 30 offspring of parents with T2D, 30 offspring of parents with impaired glucose tolerance, and 30 age- and sex-matched healthy controls. Pulse wave velocity and augmentation index were utilized to assess arterial stiffness. The results revealed that healthy offspring of parents with T2D had higher pulse wave velocity and augmentation index than the other two groups. The data suggests that early manifestation of arterial stiffness are high correlated with family history of T2D and that FH+ individuals are potentially at greater risk for vascular disease regardless of metabolic aberrations.

Arterial distensibility is a measure of an arteries' ability to expand and contract. Diabetes is associated with reduced arterial distensibility. To investigate whether this phenomenon occurs

in healthy normotensive offspring of parents with T2D, Giannattasio et al. (2008) recruited 54 healthy offspring of 2 parents with T2D and 55 age- and sex-matched controls with no family history of T2D. Carotid diameter changes, wall thickness, pulse pressure, blood pressure, blood glucose, glycohemoglobin, insulin sensitivity, brachial and arterial distensibility were assessed. Compared to the controls, FH+ participants showed reduced increases in carotid diameter during systole, increased pulse pressure, and reduced carotid artery distensibility. These data suggest that alterations in arterial mechanical properties are present in those who are predisposed to T2D.

Grassi et al. (2012) investigated the effects of dark chocolate, rich in flavonoids, on blood flow mediated dilation, blood pressure, wave reflection, and oxidative stress, before and after an oral glucose tolerance test (OGTT). Twelve healthy participants received one of the two interventions at random, 100-g of dark chocolate or flavanol-free white chocolate for 3 days. After a 7-day washout period, volunteers consumed the other chocolate. Dark chocolate ingestion significantly improved flow-mediated dilation, wave reflections, endothelin-1 and 8-iso-PGF(2α) when compared to white chocolate. However, ingesting white chocolate reduced flow-mediated dilation after an OGTT. Similarly, after white chocolate but not after dark chocolate, wave reflections, blood pressure, and endothelin-1 and 8-iso-PGF(2α) increased after OGTT. OGTT causes acute, transient impairment of endothelial function and oxidative stress, which is attenuated by flavanol-rich dark chocolate. These results suggest cocoa flavanols may contribute to vascular health by reducing the postprandial impairment of arterial function associated with the pathogenesis of atherosclerosis.

Horton et al. (2019) investigated the effects of acute hyperglycemia (AH) and hyperinsulinemia on carotid-femoral arterial stiffness. Nine healthy participants received 2 1-mU/kg/minute 2-hour insulin clamp. On one testing day, the participants were euglycemic (EH);

and on the second testing day, they were hyperglycemic (~200 mg/dL) (HH) for 2 hours before and throughout the insulin clamp. Octreotide was infused to blocked endogenous insulin. Endothelial function was assessed by flow-mediated dilation (FMD) while arterial stiffness was assessed by pulse wave velocity (PWV) and augmentation index (AI). Insulin increased carotid femoral PWV but decreased AI during HH, with AI significantly reduced in HH compared to EH. Insulin recruited microvasculature with either EH or HH, and microvascular blood volume and blood flow significantly increased in skeletal muscle after HH. No changes were observed in FMD or cardiac microvascular perfusion with either condition. This study demonstrates that AH arouses insulin-induced increases in carotid femoral arterial stiffness and that insulin's ability to recruit microvasculature is preserved during AH in healthy participants

Gordin et al. (2016) sought to investigate whether postprandial hyperglycemia affects arterial function in patients with T2DM. Three groups of male patients were included in the study; T2DM patients with albuminuria, T2DM patients without albuminuria, and healthy individuals to serve as a control. Patients ingested breakfast and were randomly assigned an insulin injection or no insulin injection. Arterial stiffness was tested using pulse wave velocity (PWV) and augmentation index (AIx) using the non-invasive method of applanation tonometry. PWV and AIx were assessed 30 minutes before breakfast and every 60 minutes after breakfast for up to 2 hours. At baseline, arterial stiffness was increased in patients. Both diabetic groups demonstrated higher brachial PWV when they were given the insulin injection and when they were not given the injection. Endothelin-1 and IL-6 were shown to be more prevalent during postprandial hyperglycemia in the T2D participants when compared to the healthy individuals. In patients with T2D and albuminuria, brachial PWV was higher under postprandial hyperglycemic conditions

when compared to the healthy control group. In short, the results suggest that hyperglycemia induces greater arterial stiffness in those who are diabetic.

Koboyashi et al. (2020) observed the effects of increasing physical activity on arterial stiffness during hyperglycemia. Nineteen elderly patients participated in the study. The research team randomly assigned 10 participants into the physical activity increase (PAI) group where they were instructed to increase their everyday physical activity, irrespective of the time or intensity, for 1 month while the remaining nine participants had to maintain their level of activity (CON). A 75-g OGTT was administered to each participant in both groups prior to and after the 1-month intervention period. After the CON group received the OGTT, brachial ankle PWV and cardio-ankle vascular index significantly increased. These increases were not seen in the PAI group. What Koboyashi and his team found suggests that a short-term increases in physical activity can attenuate the increase in arterial stiffness after glucose intake.

Acute Vascular Responses to Mixed Meal Challenge

Early detection of elevated central blood pressure and arterial stiffness are often correlated with increased peripheral blood pressure as well as increased sympathetic nervous system activity. One prominent sympathoexcitatory stimulus is the consumption of a meal. To establish whether a meal acutely affects aortic wave reflection and stiffness, Taylor et al. (2014) investigated the acute effects of a liquid mixed meal on aortic wave reflection and stiffness in 17 healthy normotensive individuals. Applanation tonometry was utilized to assess radial arterial pressure and carotid-femoral pulse velocity before, 60 minutes, and 180 minutes after the consumption of a mixed meal drink. Despite having increased sympathetic activity after the meal, peripheral and central pressures were reduced at 180 minutes pose meal consumption. Interestingly, augmentation index,

augmentation index adjusted for heart rate, augmentation pressure, and pulse wave velocity all decreased at both time points after the mixed meal drink. This is indicative of normal central hemodynamics in healthy adults which may have resulted from increases in insulin induced vasodilation.

Microvascular blood flow increases in skeletal muscle postprandially, facilitating glucose disposal. This vascular action is blunted in those who have type 2 diabetes or overweight/obese. To detect early vascular impairments, Russell et al. (2021) aimed at determining whether healthy offspring of type 2 diabetics display impaired skeletal muscle microvascular responses to a mixed meal challenge (MMC). Three groups of individuals were recruited for this study; 1) those with no family history for two generations (FH-) (n=18), 2) individuals with either parent being diagnosed with type 2 diabetes (FH+) (n=16), and 3) individuals with type 2 diabetes (n=12). All participants were administered a 75-g oral glucose tolerance test then underwent metabolic response testing by having their blood glucose, plasma insulin, and metabolic flexibility assessed before, during, and after the administration of an MMC. Skeletal muscle large artery and microvascular responses were also assessed at rest and an hour after consuming the MMC. FH+ individuals demonstrated impaired metabolic flexibility and increased microvascular blood volume after consuming the MMC. FH+ individuals were shown to have significant increases in microvascular blood flow, brachial artery blood flow and diameter as well as reduced vascular resistance. These changes were absent in both the FH+ and type 2 diabetes group. The data of this study suggests that those with a first degree relative with type 2 diabetes display impaired responses in skeletal muscle micro- and macrovascular responses after the consumption of an MMC.

Like the previous study, Caballero et al. (1999) assessed micro- and macrovascular responsiveness in four comparable groups: healthy participants with no family history of type 2 diabetes (n=30), healthy, normoglycemic individuals with either parent diagnosed with type 2 diabetes (n=39), participants with impaired glucose tolerance (n=32), and individuals with type 2 diabetes without any vascular complications (n=42). Participants underwent laser doppler perfusion imaging to assess forearm vasodilation. High-resolution ultrasounds were taken to measure brachial artery diameter changes during hyperemia. Endothelin-1, soluble intercellular adhesion molecule, soluble vascular cell adhesion molecule, and von Willebrand factor were also assessed to indicate endothelial cell function and activation. Vasodilatory responses in FH+ individuals, individuals with impaired glucose tolerance, and diabetics were blunted compared to the healthy control group. Brachial artery diameter response to hyperemia was also blunted in the groups. One important finding of this study is that an inverse correlation was found between microvascular reactivity and systolic blood pressure, glucose concentrations, insulin concentrations, and high-density lipoprotein concentrations. Additionally, brachial artery diameter changes were significantly correlated with systolic blood pressure, HbA1c, and HDL cholesterol. Of the metabolites measured, soluble vascular cell adhesion molecule was higher in both the FH+ group and type 2 diabetes group. In conclusion, the results of this study suggest that there is abnormal vascular reactivity and endothelial cell function in FH+ individuals even while these individuals display normal glucose tolerance.

CHAPTER III

Methodology

Purpose

While type 2 diabetics and prediabetics exhibit cardiovascular dysfunction, is not known whether any discrepancies exist between Hispanics from the RGV with a family history of T2D. Taking into consideration that the population of interest reside in an obesogenic and diabetogenic environment the purpose of this study is to 1) examine hemodynamics at rest and after administration of a mixed meal challenge and 2) determine whether a family history of T2D impacts cardiovascular function in otherwise healthy Hispanics.

Participants

43 participants were recruited to participate in this study. Of the 43, 12 were removed from the study as their BMI was above 30 kg/m², did not have a first-degree relative with T2D (but rather had a close relative with T2D), or did not complete the session. The remaining 31 participants between the ages of 18 – 40 that were included in this study (FH+ =15) (FH- =16) underwent the same intervention (within subject design). The University of Texas Rio Grande Valley Institutional Review Board approved the study procedure for Human Subjects. The length of each familiarization session lasted 30 minutes whereas testing sessions lasted 1 hour and 30 minutes.

Inclusion Criteria

1. Participants between the age of 18-40.
2. Participants who had no medical history of hypertension, cardiovascular disease, respiratory disease, joint or muscle problems, any metabolic disease, chronic pain.
3. Individuals with no family history of type 2 diabetes for two generations (parents or grandparents) (FH- group only).
4. Individuals with a either parent diagnosed with type 2 diabetes.

Exclusion Criteria

1. Exclusion criteria includes sustaining any muscular injury in the past 6 months and history of insulin resistance.
2. BMI >30 kg/m², history of smoking, cardiovascular disease, stroke, myocardial infarction, uncontrolled hypertension (seated brachial blood pressure >160/100 mmHg), peripheral artery disease, pulmonary disease, arthritis/muscular skeletal disease, malignancy within the past 5 years, or severe liver disease.
3. Participants ingesting medication that may interfere with cardiovascular function.
4. Individuals younger than 18 or older than 40.

Recruitment

Participants were recruited from The University of Texas Rio Grande Valley and surrounding communities through flyers and word of mouth. Participation in this study was voluntary and participants could withdraw from the study at any time

Experimental Protocol

The first session consisted of reading and signing informed consent forms, health questionnaires, 3-day food log, food questionnaire, and a physical activity readiness questionnaire. Participants underwent a whole-body scan by Dual X-ray Absorptiometry (DXA) to assess total body fat, total body fat percentage, trunk fat, android fat, and lean mass. The following session required participants to arrive to the Cardiometabolic Exercise Lab fasted for at least 10 hours. Strenuous exercise, alcohol, and caffeine were all avoided 48 hours before the visit. Participants arrived then had their height and weight assessed. Participants were then instructed rest in the supine position for 30 minutes. Pulse wave analysis (PWA) was conducted after 30-minute rest. PWA was conducted twice at least 1 minute apart. After completion of the first PWA, participants were instructed to ingest an MMC in under 1 minute. The MMC consisted of 30g of protein, 5g of fat, and 35g of carbohydrate. 60 minutes after MMC ingestion, PWA was assessed once more.

Instruments

Seca 769 Electronic Column Scale. The Seca 769 was utilized to assess height and weight All participants were required to take off unnecessary clothing, jewelry, and shoes prior to standing on the scale. The weight was recorded in both kilograms and pounds. The scale also provided BMI. Height was assessed after recording weight. Participants were instructed to look forward and breathe in deeply as the marker was lowered to the top of the participants' head. Height was recorded in centimeters.

Dual X-ray Absorptiometry (DXA). Participants underwent a whole-body DXA scan (General Electric Lunar Prodigy). Parameters that were attained included total body fat, total body fat percentage, trunk fat, android fat, and lean mass.

SphygmoCor® XCEL Pulse Wave Analyzer. The SphygmoCor XCEL was used to assess participants cardiovascular function and health using a standard arm cuff to measure brachial systolic and diastolic pressures as well as to capture a brachial artery waveform. Brachial artery waveforms are analyzed by SphygmoCor to provide a central aortic waveforms and central blood pressure measurements such as central aortic systolic and diastolic blood pressure, central pulse pressure, augmentation pressure, and aortic augmentation index (AIx) (AtCor Medical Pty. Ltd., Sydney Australia).

Statistical Analysis

A 2-way analysis of variance (ANOVA) (CATEGORY FH- vs. FH+ x TIME varied by variables) with repeated measures and pairwise Bonferroni-adjusted estimated marginal means were used to determine significant differences for variables used for analysis. Mauchly's Test of Sphericity was used on all repeated measures data to evaluate whether the sphericity assumption had been violated. If violated, Greenhouse-Geisser adjustment of degrees of freedom was

implemented. An alpha of 0.05 was used to determine statistical significance and data was analyzed using SPSS 22.0 (IBM 23 Corporation, New York, NY, USA) and Microsoft Excel 2022 for Windows (Redmond, WA, USA).

CHAPTER IV

RESULTS

Purpose

While type 2 diabetics and prediabetics exhibit cardiovascular dysfunction, is not known whether any discrepancies exist between Hispanics from the RGV with a family history of T2D. Taking into consideration that the population of interest reside in an obesogenic and diabetogenic environment the purpose of this study is to 1) examine hemodynamics at rest and after administration of a mixed meal challenge and 2) determine whether a family history of T2D impacts cardiovascular function in otherwise healthy Hispanics.

Participant Characteristics

31 participants between the ages of 18 – 60 were needed to conduct this study (FH+ =15) (FH- =16). Table 1 shows descriptive statistics that were taken from the study population.

Table 1. Participant Characteristics.

	FH-	FH+	Total
Male	10	12	22
Female	10	8	18
Age (years)	23.9 (±4.6)	28.0 (±8.8)	25.9 (±7.2)
Height (cm)	165.8 (±9.2)	168.6 (±7.0)	167.1 (±8.2)
Weight (kg)	72.2 (±13.1)	75.5 (±15.7)	73.8 9 (±14.3)
BMI (kg/m^2)	26.2 (±3.1)	26.3 (±4.1)	26.2 (±3.6)
Body Fat (%)	29.2 (±8.9)	31.4 (±11.3)	30.3 (±10.2)
Android Fat (%)	30.0 (±10.4)	35.9 (±15.2)	32.2 (±11.5)
Android Fat (g)	1404.6 (±567.4)	2136.7 (±1444.9) #	3353.1 (±880.6)
Glucose (mmol/L)	3.75 (±0.49)	3.49 (±0.50)	3.61 (±0.50)
Cholesterol (mg/dl)	147.7 (±24.9)	158.9 (±36.4)	153.3 (±31.3)
TG (mg/dl)	59.9 (±39.9)	89.4 (±30.0) #	79.2 (±36.4)
HDL (mg/dl)	45.6 (±9.2)	43.6 (±13.2)	44.6 (±11.3)
LDL (mg/dl)	84.7 (±29.0)	101.8 (±28.5)	93.4 (±29.6)
BMD (g/cm^2)	1.30 (±0.13)	1.26 (±0.09)	1.3 (±0.1)

Values are reported as means (±SE). #($p<0.05$), Significantly Different from FH-. BMI = Body Mass Index. TG = Triglycerides. HDL = High-Density Lipoprotein. LDL = Low-Density Lipoprotein. BMD = Bone Minera Density.

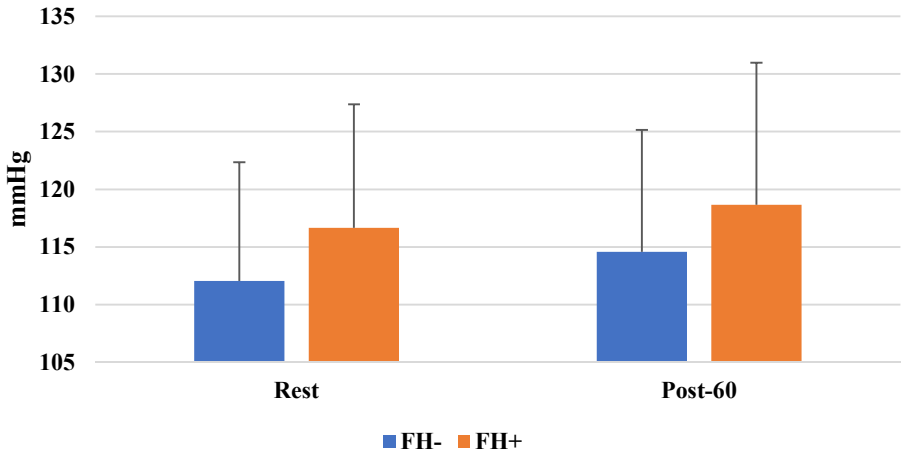

Figure 1. Brachial Systolic Blood Pressure at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 1 shows the effects of MMC on FH- and FH+ brachial systolic blood pressure. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed no main effects for time ($p=.703$) and category ($p=.959$).

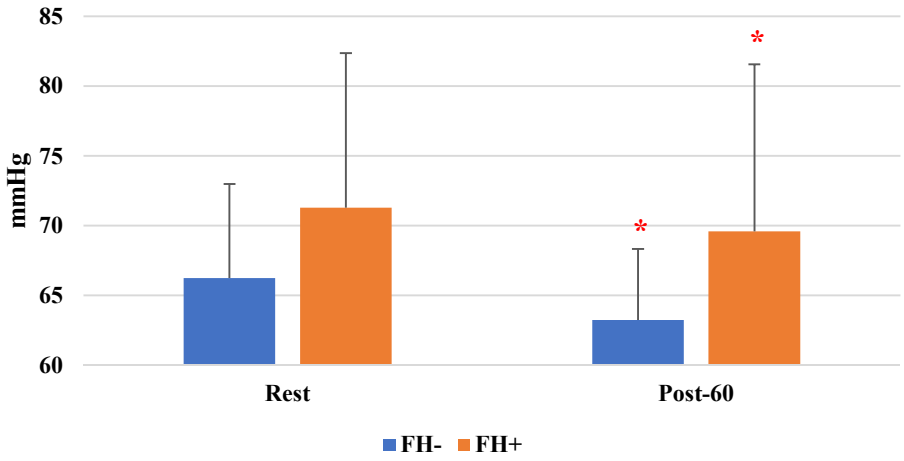

Figure 2. Brachial Diastolic Blood Pressure at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 2 shows the effects of MMC on FH- and FH+ brachial diastolic blood pressure. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed main effects for time ($p=0.015$) and but not for category ($p=.415$). Pairwise comparison for time showed a significant difference from rest to 1 hour after MMC consumption ($p=0.015$). Pairwise comparison for category showed no significant difference from rest to 1 hour after MMC consumption ($p=0.074$).

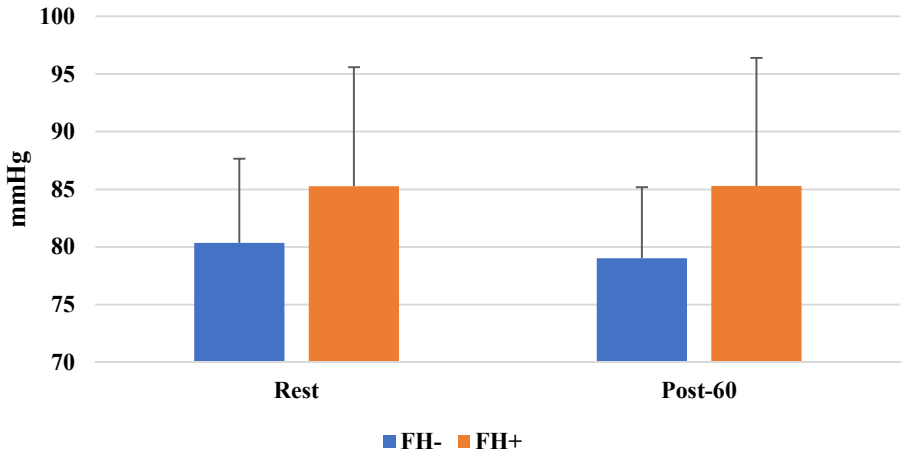

Figure 3. Mean Arterial Pressure at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 3 shows the effects of MMC on FH- and FH+ mean arterial pressure. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed no main effects for time ($p=0.415$) and category ($p=.402$).

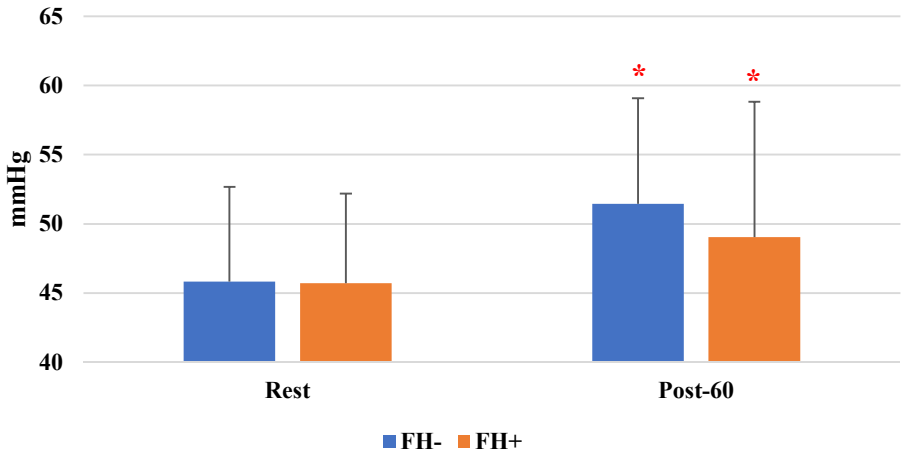

Figure 4. Peripheral Pulse Pressure at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 4 shows the effects of MMC on FH- and FH+ peripheral pulse pressure. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed main effects for time ($p=0.000$) but not for category ($p=.298$). Pairwise comparison for time showed a significant difference from rest to 1 hour after MMC consumption ($p=0.000$). Pairwise comparison for category showed no significant difference from rest to 1 hour after MMC consumption ($p=0.737$).

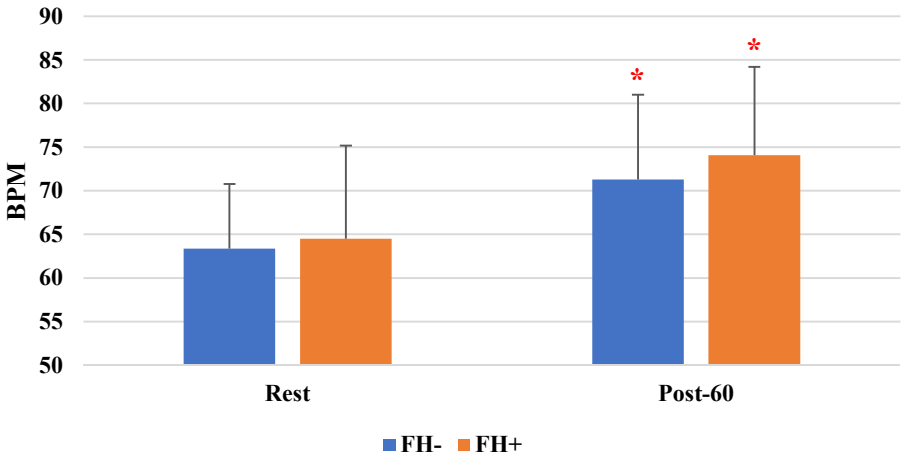

Figure 5. Heart Rate at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 5 shows the effects of MMC on FH- and FH+ heart rate. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed main effects for time ($p=0.000$) but not for category ($p=.362$). Pairwise comparison for time showed a significant difference from rest to 1 hour after MMC consumption ($p=0.000$). Pairwise comparison for category showed no significant difference from rest to 1 hour after MMC consumption ($p=.474$)

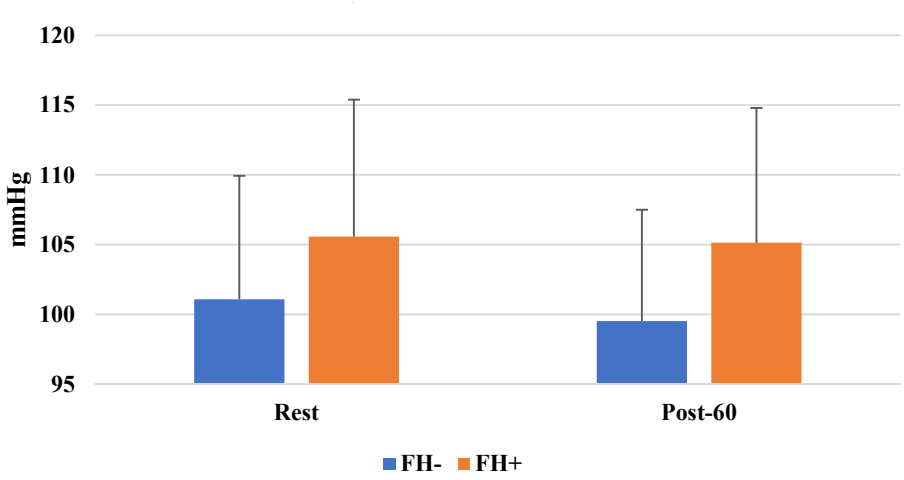

Figure 6. Central Systolic Blood Pressure at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 6 shows the effects of MMC on FH- and FH+ central systolic blood pressure. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed no main effects for time ($p=0.273$) and category ($p=.508$).

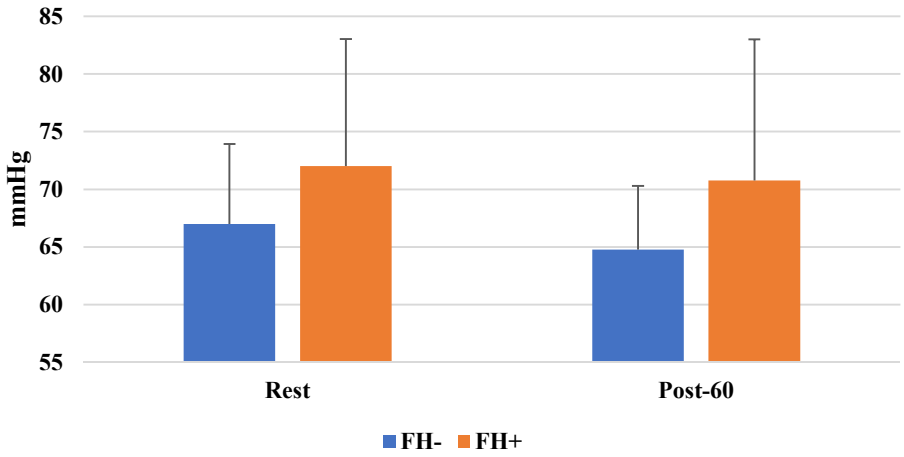

Figure 7. Central Diastolic Blood Pressure at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 6 shows the effects of MMC on FH- and FH+ central diastolic blood pressure. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed no main effects for time ($p=0.073$) and category ($p=.528$).

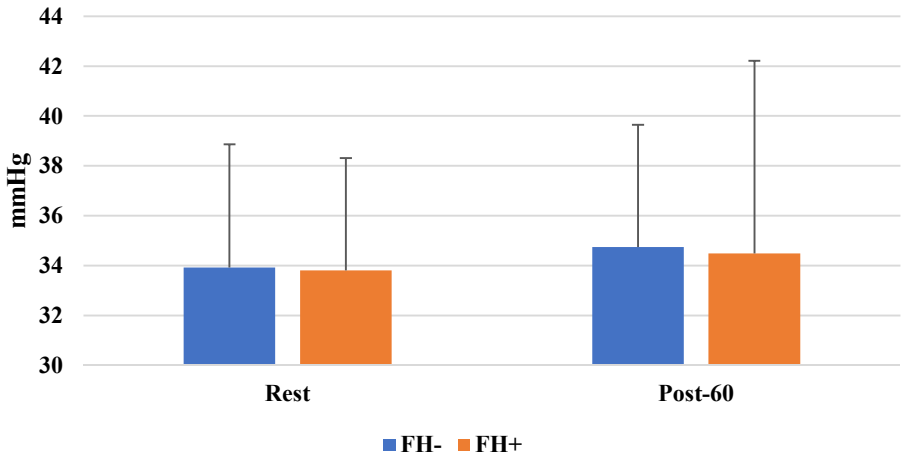

Figure 8. Central Pulse Pressure at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 6 shows the effects of MMC on FH- and FH+ central pulse pressure. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed no main effects for time ($p=0.417$) and category ($p=.908$).

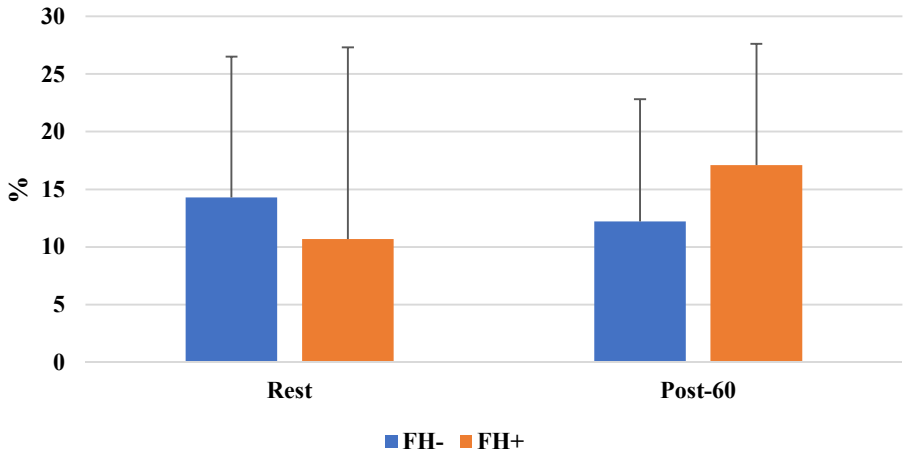

Figure 9. Augmentation Index @ 75 BPM at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 6 shows the effects of MMC on FH- and FH+ augmentation index @ 75BPM. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed no main effects for time ($p=0.633$) and category ($p=.357$).

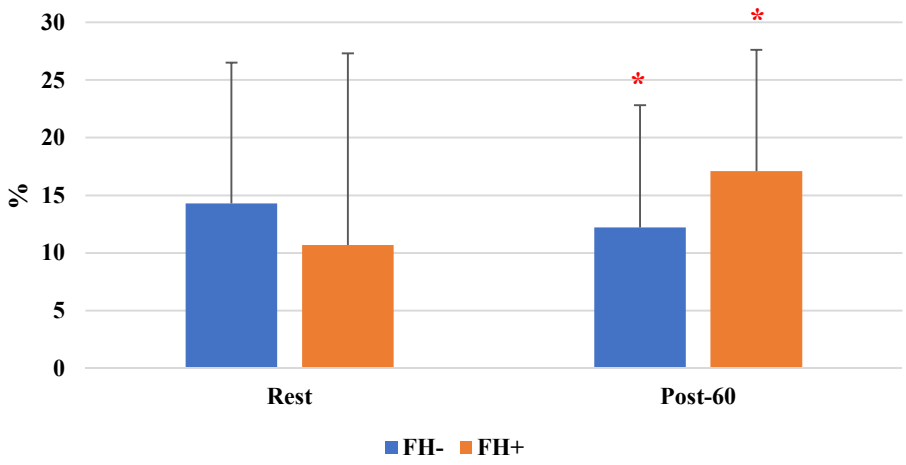

Figure 10. Augmentation Index at Rest and Post MMC Ingestion.
Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 6 shows the effects of MMC on FH- and FH+ augmentation index. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed no main effects for time ($p=0.006$) but not for category ($p=.357$). Pairwise comparison for time showed a significant difference from rest to 1 hour after MMC consumption ($p=0.006$). Pairwise comparison for category did not show a significant difference from rest to 1 hour after MMC consumption ($p=0.380$).

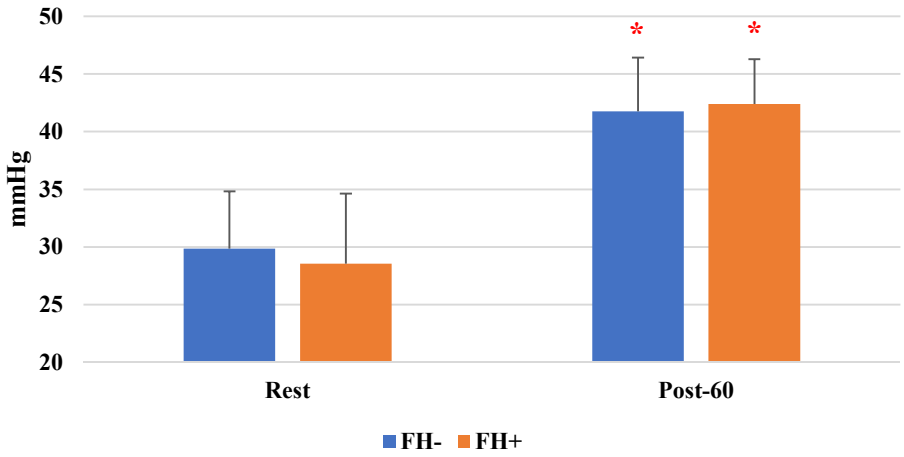

Figure 11. P1 Height at Rest and Post MMC Ingestion.

Values are reported as means (±SE). *($p<0.05$), Significantly Different from Rest. #($p<0.05$), Significantly Different from FH-.

Figure 6 shows the effects of MMC on FH- and FH+ P1 Height. Both categories were statistically similar ($p>.05$) for all effects and interactions. Repeated measures ANOVA showed main effects for time ($p=0.000$) but not for category ($p=.234$). Pairwise comparison for time showed a significant difference from rest to 1 hour after MMC consumption ($p=0.000$). Pairwise comparison for category did not show a significant difference from rest to 1 hour after MMC consumption ($p=0.914$).

CHAPTER V

DISCUSSION

Purpose

While type 2 diabetics and prediabetics exhibit cardiovascular dysfunction, is not known whether any discrepancies exist between Hispanics from the RGV with a family history of T2D. Taking into consideration that the population of interest reside in an obesogenic and diabetogenic environment the purpose of this study is to 1) examine hemodynamics at rest and after administration of a mixed meal challenge and 2) determine whether a family history of T2D impacts cardiovascular function in otherwise healthy Hispanics.

Hemodynamic & Pulse Wave Reflection Comparisons

In the present study, otherwise healthy Hispanic individuals from the Rio Grande Valley with a family history of Type 2 Diabetes displayed higher brachial and central blood pressures compared to Hispanics without a family history. However, these elevated pressures were not significantly different. These findings are contrary to other results in studies conducted by Caballero et al. (1999), Giannattasio et al. (2008), Russell et al. (2021), and Solanki et al. (2018). Being underpowered could have prevented finding significance across categories. The present study did not utilize pulse wave velocity to assess arterial stiffness. Instead, other surrogate measures were utilized such as augmentation index and augmentation index adjusted for normalized heart rate (AIx@75). Had the use of pulse wave velocity been implemented, vascular function could have been assessed further.

Conclusion

While type 2 diabetics and prediabetics exhibit cardiovascular dysfunction, is not known whether any discrepancies exist between Hispanics from the RGV with a family history of T2D. Taking into consideration that the population of interest reside in an obesogenic and diabetogenic environment the purpose of this study is to 1) examine hemodynamics at rest and after administration of a mixed meal challenge and 2) determine whether a family history of T2D impacts cardiovascular function in otherwise healthy Hispanics.

The research questions were:

3. Will there be significant divergent responses between individuals with and without a family history of T2D at rest?
4. Will there be significant divergent responses between individuals with and without a family history of T2D after MMC ingestion?

Hypothesis 1: The FH+ group will show higher pulse wave reflection compared to FH-.

While the FH- often showed lower pulse wave reflection values, it was not statistically different compared to FH+.

Hypothesis 2: The FH+ group will display higher hemodynamic pressures.

While pressures were higher in FH+ group, it was not statistically different compared to FH-. In fact, most responses were similar across groups, but the difference between these responses were not significant.

In conclusion, this study shows that otherwise healthy Hispanic FH+ individuals from the Rio Grande Valley do not display divergent hemodynamic responses before and after a mixed meal

challenge. While all blood chemistries were withing normal ranges, it appears that family history does not have an impact on vascular function in Hispanics form the Rio Grande Valley. These results are contrary to what others have found. Future research should include more participants, incorporate pulse wave velocity, and also account for nutrition and physical activity of Hispanics in the Rio Grande Valley.

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APPENDIX A

APPENDIX A

DEFINITIONS

Operational Definitions

To aid the reader, the following terms are defined as used in this study:

23. **OGC/OGTT:** Oral Glucose Challenge/Oral Glucose Tolerance Test is a lab test to check how quickly an individuals' cardiometabolic system disposes of glucose from the blood into tissues metabolically active areas such as the skeletal muscle. The test is often used to diagnose diabetes.
24. **MMC:** Mixed Meal Challenge is a test to check how much insulin an individual produces after drinking the liquid meal beverage that contains fats, protein, and carbohydrates. The MMC in this study was comprised of 35g of protein, 5g of fat, and 30g of carbohydrates.
25. **PWA:** Noninvasive assessment technique that measures peripheral blood pressure waveforms and generation of the ensuing central waveform. Using data from the previous waveforms, augmentation index and central pressure can be attained.
26. **PWV:** Pulse Wave Velocity is a noninvasive assessment of the rate at which pressure waves travel down a vessel.
27. **AIx:** Augmentation Index assesses wave reflection and arterial stiffness and calculated as a ratio. This ratio is derived from the central pulse pressure and reflected pulse pressure.
28. **Hemodynamics:** Noninvasive analysis of the pulsatile driving pressures induced by the heart, flow characteristics of blood, and mechanical properties of the vessels.

29. **FH+:** Individuals with a first degree relative diagnosed with T2D.

30. **FH-:** Individuals with no family history of T2D for 2 generations.

31. **bSBP:** Brachial Systolic Blood Pressure

32. **bDBP:** Brachial Diastolic Blood Pressure

33. **bMAP:** Brachial Mean Arterial Pressure

34. **bPP:** Brachial Pulse Pressure

35. **HR:** Heart Rate

36. **cSBP:** Central Systolic Blood Pressure

37. **cDBP**: Central Diastolic Blood Pressure

38. **cPP:** Central Pulse Pressure

39. **AIx:** Augmentation Index

40. **AIx@75:** Augmentation Index adjusted for normal heart rate

41. **AP:** Augmentation Pressure

42. **RM:** Reflection Magnitude

43. **ED:** Ejection Duration

44. **BaDia:** Brachial Artery Diameter

APPENDIX B

APPENDIX B

CONSENT FORM

The University of Texas Rio Grande Valley

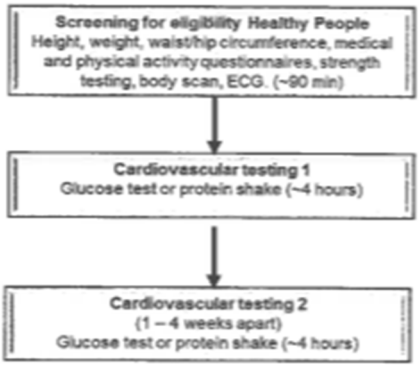
Informed Consent Form

[Cardiometabolic health in adult Latinos with and without a family history of type 2 diabetes.]

Investigators: *Ryan Russell, PhD; Murat Karabulut, PhD; Merrill Funk, PhD; Jimmy Gonzales, MD; Michelle Keske, PhD.*

Background: We are studying cardiovascular (heart) and metabolic function (diabetes/pre-diabetes) in healthy adult Latinos with and without a family history of type 2 diabetes. Insulin is a hormone in the body that helps move glucose from the blood into other tissue (like muscle). When people become less sensitive to insulin, they can develop pre-diabetes or type 2 diabetes. The purpose of this study is to see if early insulin resistance in very small blood vessels (capillaries) might be related to pre-diabetes in Hispanics in the Rio Grande Valley. We will determine if measuring how well small blood vessels, large blood vessels and metabolic function can predict risk of developing diabetes and cardiovascular disease.

Procedure:
This study will be conducted over approximately 1-2 weeks, including 3 total visits. If you agree to participate in this study, you will be asked to sign the Participant Consent Form.



VISIT 1 – SCREENING VISIT
Your eligibility to participate in the study will be determined as a result of the screening visit, where you will be asked to have the following procedures done at the UTRGV, Department of Health and Human Performance CardioMetabolic Exercise (CMX lab):

- A medical/health questionnaire to confirm eligibility.
- A physical activity questionnaire.
- Your height, body weight and waist circumference measured.
- Your blood pressure measured.
- Your maximum hand grip strength (how strong your hand-grip is)

- Your blood pressure will be measured using a blood pressure cuff placed on your upper arm.
- Measures of large artery function will be done fasting, and at 60 min after consuming the Glucose or protein shake, using a probe that will be placed on the skin where large arteries can be felt (neck, wrist, hip, etc). These just touch the skin, and measure pressure in the artery each time the heart beats.
- Non-invasive measures of cardiovascular health including pictures of the heart using echocardiography and pictures of your artery in your upper arm by ultrasound.
- Blood flow in the muscle of your arm and the fat under the skin on your abdomen will be tested using ultrasound. This will require placing infusing a contrast agent into one of your veins through the IV that is in place so that pictures of these small blood vessels can be taken.
- Non-invasive measurement of your rate of metabolism. This involves placing a small plastic hood over your head to sample the air that you expire.
- Body composition measurement via Dual Energy X-ray Absorbance (DXA).
- Urine sample to measure electrolytes and oxidative stress.

'How is this study being paid for?'
The study is being sponsored by the Internal Seed Research Program (ISRP) grant at UTRGV, and by the PI's start-up funds.

'Are there risks to me in taking part in this study?'
All medical procedures involve some risk of injury. In addition, there may be unknown risks associated with this study. In spite of all precautions, there is a very small chance of developing medical complications from participating in this study. Other known risks of this study are possibly:

- Discomfort/pain associated with having blood samples taken including bruising. IV placement can result in bruising (mild, rarely severe) in the area where the IV is placed, and potentially (very rare) infection. It is possible, though unlikely, that the IV could come out of place, requiring a new IV to be placed.

- A small number of people (8.4% of people) have side-effects during the infusion of the contrast agent (Definity/Lumison) during ultrasound imaging. The most common of these side-effects include:

The University of Texas Rio Grande Valley

Informed Consent Form

Voluntary Participation: Your participation in this study is voluntary; you may stop your participation at any time without penalty. If for any reason you decide that you would like to stop your participation, simply tell the researcher that you wish to stop.

Treatment for Physical Injury: In the event that you suffer a research related injury, your medical expenses will be your responsibility or that of your third-party payer (insurance). Neither UTRGV nor any representative or employee thereof shall be held responsible for any injury or illness incurred while participating in this study. Although, you are not prevented from seeking to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research

Termination of your Participation by the Researcher: The PI (Russell) reserves the right to remove any participant from the study for any reason.

Early Withdrawal from the Study: You may withdraw from the study at any time with no consequences.

Anonymity and/or Confidentiality: Your sample will be de-identified (having no information to connect to you). De-identified samples are those collected without identifying information. There may be some limited information that is important to this research, such as sex, age, ethnicity, or health, but this information is not enough to identify you. Because samples are de-identified, employers or insurance companies will not be able to discriminate against individual participants. However, sometimes genetic research, even on de-identified samples, may reveal information about an identifiable group. Because your sample is de-identified, no personal genetic information can be provided to you. The only people who will know that you are a research subject are members of the research team and, if appropriate, your physicians and nurses. No information about you, or provided by you during the research will be disclosed to others without your written permission, except if necessary to protect your rights or welfare (for example, if you are injured and need emergency care) or if required by law. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity.

All records containing personal information, research data, and related records will be stored in locked files at UTRGV in the STDOI Freezer Farm. All data collected will be assigned with a subject identification code to protect personal privacy. This code (subject identification number) will be linked to the subject's name and date of birth and will be stored in a password protected database on a password protected computer in the CardioMetabolic Exercise Laboratory that is separate from all other data obtained within the study; this information will only be accessible to Dr. Ryan Russell's lab personnel. All data obtained from samples will be identified by the subject identification number and will not be associated with any personal identifier of the subject including the name and/or patient or student number. After all the data has been analyzed, it will be kept in storage for 10 years, and then destroyed by a paper shredder.

unless the research involves children (under which circumstances a parental informed consent and possibly child assent is needed): In order to participate, you must be at least 18 years of age. If you are under 18, please inform the researcher.

_____ ____/____/_____

Participant's Signature Date

APPENDIX C

APPENDIX C

RECRUITMENT FLYER

APPENDIX D

APPENDIX D

PHYSICAL ACTIVITY QUESTIONNAIRE

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

Microvascular regulation of metabolism in adult Latinos with and without specific gene mutations.

Instructions: Please read carefully

Please answer all questions to the best of your ability.

Your answers will be completely confidential.

Please use black or blue pen if possible.

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

   ____ **hours per day**

   ____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

   ____ **hours per day**

   ____ **minutes per day**

   ☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

APPENDIX E

APPENDIX E

GENERAL HEALTH QUESTIONNAIRE

General Health Questionnaire

Microvascular regulation of metabolism in adult Latinos with and without a specific gene mutations – Pilot Study.

Instructions: Please read carefully

Please answer all questions to the best of your ability (leave blank if unknown.) Your answers will be completely confidential.

Indicate your answer by marking the box □ to the most appropriate answer, or by writing clearly in the boxes provided.

Cross out any mistakes and write correct answers just below the relevant boxes.

Please use black or blue pen if possible.

DEMOGRAPHIC INFORMATION

Surname:		**DOB:**
Given Names:		
Gender:	☐ M ☐ F	
Ethnicity:	☐ Caucasian ☐ Aboriginal/Torres Strait Is. ☐ Asian ☐ Other	
Address:		
City/ Suburb:		
State:		
Postcode:		
Telephone:	Home:	
	Mobile:	
email:		

GENERAL PRACTITIONER DETAILS

Surname:		
Given Names:		
Address:		
City/ Suburb:		
State:		
Postcode:		
Telephone:		
Email/Fax:		

EDUCATION, EMPLOYMENT AND MARRIAGE

ALL QUESTIONS CONTAINED IN THIS SECTION ARE OPTIONAL AND WILL BE KEPT STRICTLY CONFIDENTIAL.

Work:	Which of the following describes your current employment status? (you can pick more than one)	
	☐ Working full-time	
	☐ Working part-time	
	☐ Not working (but not retired)	
	☐ Home Duties	
	☐ Full-time student	
	☐ Part-time student	
	☐ Retired	
	☐ Other (please specify)	
Occupation:		**Years spent in this occupation:**
Education:	What is the highest level of education you have completed?	
	☐ Primary	
	☐ Year 7,8,9 or equivalent	
	☐ year 10 or equivalent	
	☐ Year 11 or equivalent	
	☐ Year 12 or equivalent	
	☐ Trade/apprenticeship (e.g., hairdresser, chef)	
	☐ Certificate/diploma (e.g., child care, technician)	
	☐ University Degree	
	☐ Higher University Degree (e.g., Grad Dip, Masters, PhD)	
	☐ Other (please specify)	
Marital status:	☐ Single ☐ Partnered ☐ Married ☐ Separated ☐ Divorced ☐ Widowed	

DO YOU HAVE A FAMILY HISTORY OF TYPE 2 DIABETES?

	AGE	DIAGNOSED TYPE 2 DIABETES?	
Father		☐ Yes	☐ No
Mother		☐ Yes	☐ No
Sibling	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
Grandmother *Maternal*		☐ Yes	☐ No
Grandfather *Maternal*		☐ Yes	☐ No
Grandmother *Paternal*		☐ Yes	☐ No
Grandfather *Paternal*		☐ Yes	☐ No

DO YOU HAVE A FAMILY HEALTH HISTORY OF PREMATURE CADIOVASCULAR DISEASE

Angina, Stroke, Myocardial infarction (Males ≤55 years, Females ≤65 Years)

	AGE	PREMATURE CVD	
Father		☐ Yes	☐ No
Mother		☐ Yes	☐ No
Sibling	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
	☐ M ☐ F	☐ Yes	☐ No
Grandmother *Maternal*		☐ Yes	☐ No
Grandfather *Maternal*		☐ Yes	☐ No
Grandmother *Paternal*		☐ Yes	☐ No
Grandfather *Paternal*		☐ Yes	☐ No

MEDICATIONS

List your prescribed drugs and over-the-counter drugs, such as vitamins and inhalers

Name the Drug	Strength (dosage)	Frequency Taken	How Long have been taking this Drug (years)

Allergies to medications

Name the Drug	Reaction You Had

APPENDIX F

APPENDIX F

IRB APPROVAL LETTER

tick@lab - IRB Protocol IRB-18-0246 - 2017-094-04: Cardiometabolic health in adult Latinos in the Rio Grande Valley with and without specific gene mutations. has been approved

tickatlab@utrgv.edu <tickatlab@utrgv.edu>
Mon 11/8/2021 11:05 AM
To:

- Ryan Russell <ryan.russell@utrgv.edu>;
- Yu Lun Tai <yulun.tai@utrgv.edu>;
- Jimmy Gonzales <jimmy.gonzales@utrgv.edu>;
- Gabriel Figueroa <gabriel.a.figueroa01@utrgv.edu>

Dear tick@lab user,

The IRB protocol with ref. no. IRB-18-0246 has been approved.

Any changes/amendments to your IRB Protocol must be submitted as a revision and approved by the IRB committee prior to initiation in research activities. A copy of your official approval letter is attached to your protocol study file.

Status change comment:
This continuing review has been reviewed and approved by the UTRGV IRB.
This project will expire one year from it's previous expiration date, June 1, 2022 please submit a continuation review request prior to the expiration. Please remember to close the project via a project closure request on tick@lab once the project is completed, and submit amendments to obtain approval prior to implementing changes to your protocol. An approval letter will be published at the file level where it will always be accessible to you. This letter will note any requirements for reporting and will provide the details of this approval. To access your letter right-click on the paperclip icon at the file level (next to the file folder icon) and select Edit Attachment from the menu. Simply clicking on the document will download a copy for your records.
Please click here to open the document.

This message has been automatically generated by the tick@lab system. Please DO NOT REPLY to this message as this mailbox is unmonitored.

For questions, please contact the IRB Coordinator or your system administrator.

To access the tick@lab system, please
visit https://LAR.utrgv.edu/tickatlab/Default.aspx?module=IRB&action=List.

BIOGRAPHICAL SKETCH

Gabriel Alejandro Figueroa has earned his bachelor's degree in Exercise Science December 2019 acquired from the University of Texas at Brownsville. He went onto to attain his Master's degree in Exercise Science May 2022, also acquired from the University of Texas Rio Grande Valley. Currently, Gabriel serves as the owner of ExerScience Online Coaching, serves as a research consultant and ambassador for Outwork Nutrition, investigating the effects of different resistance exercise order on autonomic modulation and vascular function, and is working towards attaining admittance to the University of Texas Rio Grande Valley School of Medicine. Contact information: Gabriel29figueroa@gmail.com.