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Role of Carbohydrate Source as Part of a Higher Protein Diet on Markers of Metabolic Syndrome

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Role of Carbohydrate Source as Part of a Higher Protein Diet on Markers of Metabolic Syndrome

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Food Science

by
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University of Arkansas
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This thesis is approved for recommendation to the Graduate Council.

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Abstract

Obesity has become a major health crisis in the United States and across the globe [1]. Recent findings suggest that approximately 50% of U.S. adults will have obesity and 25% will have severe obesity (body mass index (BMI) > 40 kg/m²) by the year 2030 [2]. Obesity-related cardiometabolic dysfunction is a significant public health concern [3, 4]. As rates of obesity increase, so too does prevalence of the metabolic syndrome [5]. In the United States, incidence of Metabolic syndrome (MetS) is increasing, with approximately one in three adults qualifying for a diagnosis [6, 7]. MetS is a grouping of cardiometabolic risk factors including insulin resistance (IR), visceral adiposity (VA), atherogenic dyslipidemia (AD), and endothelial dysfunction (ED) [8]. Each risk factor has its own detrimental effects, however, when these risk factors are clustered together they can have an even greater impact on cardiovascular health [9]. If left untreated, the cardiometabolic risk factors of MetS contribute to the pathogenesis of cardiovascular disease (CVD) and type 2 diabetes (T2D) [10]. Currently, there are two primary approaches used to treat and manage MetS: pharmacological and lifestyle (e.g. physical activity, nutrition/dietary intake) modification [11]. Recently, higher protein diets (HPD) (approximately 28–30% of macronutrient content) and their effects on biomarkers of MetS have been the subject of much investigation [12–22]. Studies performed to evaluate short-term (4–24 hours) consumption of HPD show that HPD result in appetite suppression through decreased levels of orexigenic hormones and increased level of anorexigenic hormones, elevated plasma amino acid levels, increased hepatic gluconeogenesis, and increased ketogenesis from the higher protein intake and increased energy expenditure through increased diet-induced thermogenesis [23, 24]. Studies performed to evaluate long-term (12–26 weeks) consumption of a HPD show that HPD

results in reduced body weight and fat mass while preserving more lean mass and increasing energy expenditure when compared to a standard protein diet (SPD) [25-30].

Most research with HPD and its effect on cardiometabolic biomarkers, focuses on consumption of HPD under conditions of weight loss. However, very few studies focus on the role of the carbohydrate source in conjunction with a HPD in a state of weight maintenance and its effects on cardiometabolic biomarkers in adults at risk for MetS. Therefore, the objective of this thesis was to determine the role of the carbohydrate source with a HPD on cardiometabolic biomarkers in adults at risk for MetS. We conducted two dietary interventions: 1) to determine the short-term effects of a carbohydrate source with a HPD on biomarkers in adults at risk for MetS and 2) to determine the long-term effect of a carbohydrate source with a HPD on cardiometabolic biomarkers in adults at risk for MetS. We hypothesized that 1) HPD containing white potatoes will improve appetite response in adults at risk for MetS and 2) HPD containing white potatoes will improve cardiometabolic biomarkers in adults at risk for MetS when compared to a HPD containing a control carbohydrate (white rice/pasta).

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Dedication

This thesis is dedicated my loving parents, Nathan Daniel Thomas and Amanda Olsen Thomas, as well as the numerous friends and family who continue to encourage me. Thank you for your steadfast support throughout my endeavors.

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Abbreviations

AD – atherogenic dyslipidemia

ASCVD – atherosclerotic cardiovascular disease

BMC – bone mineral content

BMD – bone mineral density

BMI – body mass index

CVD – cardiovascular disease

DEXA – dual-energy x-ray absorptiometry

ED – endothelial dysfunction

FFA – free fatty acid(s)

HDL – high-density lipoprotein

HOMA-IR – homeostatic model of assessment for insulin resistance

HPCC – higher protein, control carbohydrate

HPD – higher protein diet(s)

HPWP – higher protein, white potato

IDF – International Diabetes Federation

IFG – impaired fasting glucose

IGT – impaired glucose tolerance

IL-6 – interleukin-6

IR – insulin resistance

LDL – low-density lipoprotein

MetS – metabolic syndrome

NCEP (ATP III) – National Cholesterol Program (Adult Treatment Panel III)

SPD – standard protein diet(s)

TC – total cholesterol

TRG – triglycerides(s)

T2D – type 2 diabetes

VA – visceral adiposity

VAS – visual analogue scale

WC – waist circumference

WHO – World Health Organization

WHR – waist-to-hip ratio

WHtR – waist-to-height ratio

Introduction

Obesity has become a significant health problem in the United States and across the globe [1]. Recent findings suggest that approximately 50% of U.S. adults will have obesity and 25% will have severe obesity (body mass index (BMI) > 40 kg/m²) by the year 2030 [2]. As rates of obesity increase, so too does prevalence obesity-related diseases, such as the metabolic syndrome [5]. Metabolic syndrome (MetS) is a clustering of cardiometabolic risk factors including insulin resistance (IR), visceral adiposity (VA), atherogenic dyslipidemia (AD), and endothelial dysfunction (ED) [8]. Each risk factor has its own detrimental effects, however, when these risk factors are grouped together they can have an even greater impact [9]. Globally, prevalence of MetS has reached 31%, and is associated with a 1.5-fold increase in the risk of all-cause mortality [31]. If left untreated, the cardiometabolic risk factors of MetS aid in the development of cardiovascular disease (CVD) and type 2 diabetes (T2D) [10].

Currently, there are two primary approaches used to treat and manage MetS: pharmacological and lifestyle (e.g. physical activity, nutrition/dietary intake) modification [11]. Recently, higher protein diets (HPD) have been the subject of much investigation [12-22]. The current recommended dietary allowance (RDA) for protein is 0.8 g/kg body weight/day [32]. However, researchers suggest that the daily recommendation for protein intake should be increased to 20-35% of macronutrient intake, as the benefits of protein intake beyond the RDA are well-established [33-38].

Studies have shown that consumption of HPD have resulted in reduced body weight and fat mass while preserving more lean mass and increasing energy expenditure when compared to a standard protein diet (SPD) under caloric restriction [24, 39, 40]. In a study evaluating

performance of a HPD (25% of macronutrient intake) or SPD (15% of macronutrient intake) in a 12 week dietary intervention study evaluating 43 overweight and obese men, researchers found that consumption of a HPD aided in the preservation of more muscle mass while experiencing weight loss compared to a standard protein diet [41]. One systematic review and meta-analysis evaluated the effects of high-protein, low fat diets (25-35% protein, < 30% fat) compared to standard-protein, low-fat diets (12-18% protein, < 30% fat) on weight loss, body composition, resting energy expenditure, satiety and appetite, and cardiometabolic biomarkers and found that isocalorically prescribed high-protein, low-fat diet showed notable benefits for weight loss, fat loss, and reduction in TRG, while mitigating reductions in fat-free mass [25].

Currently, there has been a significant amount of research focused on HPD and its effect on cardiometabolic biomarkers under caloric restriction however, very few studies have investigated the role of 1) HPD on markers of cardiometabolic health during weight maintenance, and 2) the impact of carbohydrate source in conjunction with a HPD on cardiometabolic biomarkers in adults at risk for MetS. Therefore, the overall goal of this thesis was to determine the role of the carbohydrate source with a HPD on cardiometabolic biomarkers in adults at risk for MetS.

The objectives of this study are as follows:

Objective 1: Determine the short-term effects of a carbohydrate source with a HPD on biomarkers in adults at risk for MetS.

Objective 2: Determine the long-term effect of a carbohydrate source with a HPD on cardiometabolic biomarkers in adults at risk for MetS.

We hypothesized:

Hypothesis 1: HPD containing white potatoes will improve appetite response in adults at risk for MetS.

Hypothesis 2: HPD containing white potatoes will improve cardiometabolic biomarkers in adults at risk for MetS.

Chapter 1: Literature Review

Introduction

Obesity has become a major health crisis in the United States and across the globe [1]. Recent findings suggest that approximately 50% of U.S. adults will have obesity and 25% will have severe obesity (body mass index (BMI) > 40 kg/m²) by the year 2030 [2]. As rates of obesity increase, so too does prevalence of the metabolic syndrome [5]. Metabolic syndrome (MetS) is a grouping of cardiometabolic risk factors including insulin resistance (IR), visceral adiposity (VA), atherogenic dyslipidemia (AD), and endothelial dysfunction (ED) [8]. If left untreated, the cardiometabolic risk factors of MetS aid in the pathogenesis of cardiovascular disease (CVD) and type 2 diabetes (T2D) [10].

Obesity-related cardiometabolic dysfunction is a significant public health concern [3, 4]. As of 2018, MetS was estimated to affect as much as 25% of the global population [7]. Often, incidence of MetS coincides with obesity and type 2 diabetes (T2D) [42]. In fact, the first internationally recognized definition of MetS originated from the diabetes consultation group of the World Health Organization (WHO) in 1998 [43, 44]. Currently, there are several accepted definitions of MetS [45]. The three most widely used definitions in surveys and healthcare are the WHO 1999 definition, the NCEP ATP III 2005 definition, and the International Diabetes Federation (IDF) 2006 definition (See **Table 1**) [46]. According to the WHO definition, insulin resistance is a mandatory criterion for MetS, with obesity, dyslipidemia, and hypertension being secondary [47]. Oppositely, the IDF definition requires that obesity, but not necessarily insulin resistance, be present [48]. However, the remainder of the criteria outlined in the IDF definition are similar to that of the WHO definition [49]. The NCEP ATP III definition states: MetS is

present if three or more of the following five criteria are met: waist circumference over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting triglyceride (TRG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl [50]. The definition for MetS outlined in the NCEP ATP III report is the most widely accepted and easy-to-use set of criteria to date, as it utilizes laboratory measurements that are readily available in a clinical setting [8].

There is strong association between MetS and increased risk of developing CVD [50]. According to The National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP III) report, CVD is considered the primary outcome of MetS if left untreated [43, 51]. In the United States, incidence of MetS is high and increasing, with approximately one in three adults qualifying for a diagnosis [6, 7]. Incidence of insulin resistance and MetS is estimated to be approximately 31% in the U.S. and range from 20-40% in developing countries and continues to increase [52-54]. In 1995, Reaven was the first to suggest that hyperinsulinemia as the driving physiological mechanism for the clustering of dyslipidemia, hypertension, and impaired glucose metabolism [55, 56].

The inability of insulin to adequately stimulate glucose transport into the body's cells is a key component of MetS and T2D [57, 58]. In a healthy individual, insulin binds to a ligand-activated tyrosine kinase, which results in tyrosine phosphorylation of downstream substrates and stimulation of two parallel pathways: the phosphoinositide 3-kinase (PI3K-Akt) pathway and the mitogen activated protein (MAP) kinase pathway [59]. The PI3K-Akt pathway is largely responsible for phosphorylation and activation of endothelial nitric oxide synthase (eNOS) and

translocation of GLUT4 to the surface of the cell. The MAP kinase pathway mediates endothelin-1 (ET-1) production, thus leading to vasoconstriction, growth, and mitogenesis effects on the vascular smooth muscle cells [8]. In an insulin resistant individual, the PI3K-Akt pathway is impaired, while the MAP kinase pathway remains unaffected. Properly functioning insulin impacts the body in significant ways such as: regulation of glucose uptake, gluconeogenesis, glycogen synthesis, lipid metabolism, hunger, gene expression, protein synthesis, cell growth and division, and vasodilatation [60-62]. Studies have proposed that tissues that are normally sensitive to the effects of insulin (heart, skeletal muscle, etc.) will defend against nutrient-induced toxicity by becoming insulin resistant in response to chronic overnutrition [63-65]. Obese and type 2 diabetic individuals are resistant to the biological effects of insulin in skeletal muscle, adipose tissue, and liver, whereas normal weight individuals with normal glucose tolerance are highly sensitive to insulin in those areas [66-70]. Currently, the “gold standard” for measurement of whole body insulin sensitivity is known as the euglycemic-hyperinsulinemic clamp method, however this procedure is complex and impractical for clinical use [71]. Other methods have been developed using oral glucose tolerance tests and fasting samples to measure insulin sensitivity such as the Matsuda index and the homeostatic model for assessment of IR [Homeostatic Model of Assessment-IR (HOMA-IR)] [72, 73].

Adipose tissue is an important component for the normal physiological function of the body. It functions as an energy storage organ as well as an essential and highly active endocrine organ [74]. Chronic over-nutrition will result in adipocyte hyperplasia, adipose tissue hypertrophy, or a combination of both that severely impair the overall functionality of the

organ [75]. The expansion of adipose tissue via hypertrophy (increase in adipocyte size) and hyperplasia (increase in adipocyte number) will lead to an inappropriate balance of pro- and anti-inflammatory adipokine secretion, ultimately resulting in systemic metabolic dysfunction and CVD [76, 77]. Pro-inflammatory adipokines (tumor necrosis factor alpha (TNF α), leptin, interleukin-6 (IL-6), resistin, interleukin-18 (IL-18), etc.) are upregulated with obesity, whereas anti-inflammatory adipokines (adiponectin, secreted frizzled-related sequence protein 5(SFRP5), etc.) are downregulated with obesity [78]. This means that in a state of obesity, the physiological response of pro-inflammatory adipokines is increased, while the response of anti-inflammatory adipokines is decreased, resulting in inflammation-induced IR in the body [79].

Obesity in the form of visceral adiposity plays a significant role in the development of MetS [80]. Free-fatty acids (FFA) secreted from visceral adipose tissue (VAT) and bioactive lipid mediators work together with pro-inflammatory adipokines to increase oxidative stress and compromise the PI3K-Akt pathway [81]. Anthropometric indicators such as body mass index (BMI), waist-to-height, waist circumference (WC), and waist-to-hip ratio (WHR) have been used to estimate VAT [82, 83]. As well, biochemical measurements such as plasma concentrations of TRG and high-density lipoprotein cholesterol (HDL-C) are indicative of visceral adiposity [84]. High levels of visceral adiposity and insulin resistance are also associated with abnormality of the blood serum lipid profile [85, 86].

Atherogenic dyslipidemia (AD) is a typical feature of MetS and T2D and an important risk factor of CVD [87, 88]. AD is characterized by increased plasma concentration of TRG and small-dense low-density lipoprotein cholesterol (LDL) and decreased concentration of high-density lipoprotein (HDL) cholesterol [89]. Simultaneous occurrence of these metabolic risk factors may

be associated with an adipose tissue related proinflammatory gradient that has potential effects on the endothelium [90]. Overabundance of circulating FFA, pinocytosis of TRG-rich lipoproteins, and de novo lipogenesis will result in hepatic overproduction of apoB, the major apolipoprotein of LDL [91, 92]. Penetration and retention of apoB containing lipoproteins is a fundamental step in the onset of AD [93-95]. In a healthy individual, inhibition of hormone sensitive lipase, an essential catalyst in lipid metabolism and energy homeostasis, is achieved as a result of postprandial increase of insulin [96, 97]. Inappropriate insulin signaling in the PI3K-dependent pathways will impair functional lipid metabolism by increasing lipolysis and FFA levels [86, 98].

Endothelial dysfunction (ED) is the fourth pathway leading to MetS and other CVDs [99-101]. All blood and lymphatic vessels within the vascular tree are lined with endothelial cells which aid in blood fluidity, vascular tone, and platelet aggregation—this is known as the endothelium [102]. The endothelium produces various atheroprotective vasoactive factors such as nitric oxide (NO), prostacyclin (PGI₂), thromboxane (TXA₂) and endothelin-1 (ET-1) [103-105]. Imbalanced production of these vasoconstrictive and vasodilatory factors will lead to ED [106]. More specifically, decreased amount of bioavailable NO in the vasculature will result in increased endothelial cell activation, smooth muscle proliferation, leukocyte activation and leukocyte-endothelial interactions, smooth muscle proliferation, and platelet aggregation and adhesion [107-110]. A principal mechanism for ED occurs at S1177 by reduction of eNOS phosphorylation, which increases eNOS activity, and thus, NO production [111]. In a healthy individual, functional insulin signaling leads to increased eNOS phosphorylation via the PI3K-Akt pathway, whereas an insulin resistant individual has reduced eNOS activity due to low Akt

kinase activity [112]. As well, individuals with high levels of visceral adiposity will have reduced eNOS activity due to the physiological effects of IL-6, resistin, and TNF α [113]. In contrast, stimulation of eNOS phosphorylation is diminished during MetS due to the effects of adiponectin [114].

Metabolic Syndrome and Type-2 Diabetes Mellitus

The hyperglycemic condition of individuals with MetS makes them predisposed to developing additional health complications such as T2D [115, 116]. Many investigations have assessed the relationship between MetS and T2D. For example, in the study by Nsiah et al., T2D females were three times more likely to have MetS than males (77.01% F: 22.99% M) due to notably higher rates of central obesity and lowered HDL-C levels [117], findings which have been further supported in similar studies [118, 119]. Furthermore, it is acknowledged in the literature that individuals with decreased levels of HDL-C may be at increased risk of developing coronary heart diseases or CVD [120-123]. Alternatively, another study investigating the risk of CVD, coronary heart disease, and T2D according to traits of MetS found that risk estimates associated with MetS for CVD, CHD, and T2D were 34%, 29%, and 62% in men and 16%, 8%, 47% in women, respectively [124]. It is well documented in the literature that concomitant T2D and MetS leads to increased risk of development of additional health conditions including cognitive impairment, nonalcoholic fatty liver disease, polycystic ovary syndrome (PCOS), and atherosclerotic cardiovascular disease (ASCVD) [65, 125-129]. Similarly to MetS, T2D is largely a result of decreased insulin activity [130]. Studies suggest that chronic consumption of excess glucose and lipids will lead to β cell dysfunction, eventually leading to development of T2D

[131]. Insulin resistance has been shown to anticipate the incidence of hyperglycemia, but only in individuals with the onset of β cell dysfunction [132-136].

Type 2 Diabetes Mellitus, Metabolic Profiling, and Inflammation

Currently, classification of individuals within the general population who are at risk for T2D is based on key factors such as age, BMI, and fasting glucose concentrations [137]. However, these measurements are based only on the presence of the disease and cannot identify risk before initiation of the disease process [138]. A number of studies have set out to investigate the role of several metabolites in the incidence of IR and T2D [139-143]. Metabolic profiles associated with T2D have been identified up to fifteen years before diagnosis and/or onset of the disease [144-146]. In a study of 2,204 females (115 T2D case subjects, 192 individuals with impaired fasting glucose, and 1,897 control subjects), researchers aimed to investigate novel molecular markers before and after hyperglycemia by comparing individual's fasting metabolomic profiles. Of the 447 fasting plasma metabolites analyzed, forty-two from three major fuel sources (carbohydrates, fats, and proteins) showed significant differences between T2D cases and control subjects. The branched-chain keto-acid metabolite 3-methyl-2-oxovalerate was the most significant predictive biomarker for impaired fasting glucose after and independently of glucose concentrations [138].

It is well documented that chronic low-grade inflammation and the immune system are involved in the development of IR, T2D, and metabolic dysfunction [78, 147-149]. Many pro-inflammatory markers such as C-reactive protein, TNF- α , interleukin-6 (IL-6), etc. are elevated while in a state of obesity or T2D [150-155]. As well, these inflammatory markers are also

potentially associated with IR and certain elements of MetS, often regardless of degree of adiposity [150, 152, 155-158]. Stress and inflammation determined by plasma cortisol and IL-6 concentrations are additional cardiometabolic biomarkers associated with MetS [159]. Obesity and stress are interrelated and are the subject of much research [160-163]. Recent studies have found that elevated levels of cortisol aid in the promotion of abdominal obesity [164-166]. A community-based study in 619 adults found that there is a relationship between chronic stress, food cravings, and BMI [167]. Current data suggests that increased levels of cortisol may increase stress-related eating patterns, and therefore adiposity [168, 169]. In the study of Park et al. [170], Korean men and women with increased plasma cortisol levels were found to be at an increased risk for MetS. In fact, one review outlines how high levels of cortisol increase glycogenolysis, gluconeogenesis, insulin resistance, free fatty acids, and visceral obesity, and indirectly and directly reduces insulin secretion. Collectively, these effects increase risk of MetS and T2D [171-173].

IL-6 is an inflammatory cytokine whose chronically elevated levels may also increase risk of MetS and T2D. This notion is supported in a study on 80 obese adults meeting the IDF 2007 diagnosis criteria for MetS. When comparing concentrations of adipocytokines in the studied group and control group, researchers found that patients with MetS (studied group) had significantly higher levels of proatherogenic adipokines, including IL-6 [174]. In a healthy individual, IL-6 provides many of the beneficial metabolic features associated with physical activity [175]. However, chronically elevated plasma (IL-6) concentrations have been shown to be correlated with incidence of obesity and T2D [176]. Research has shown that over production of IL-6 will result in compromised immune regulation in the adipose tissue, thus

becoming a detrimental rather than favorable cytokine in obese individuals [177-180]. In a nested case-control study including 27,548 individuals, researchers found that increased levels of circulating IL-6 were an independent risk factor for the development and progression of T2D [181]. One study set out to investigate the role of IL-6 in glucose metabolism, however, results showed no evidence that IL-6 had an effect on glucose metabolism in T2D [182]. In a watershed manuscript published by Priceman et al [183], signaling of IL-6 via the STAT3 pathway is vital for appropriate balance of pro-inflammatory T_H1 cells (cells that aid in the function of other immune cells) and Tregs (regulatory T cells) in adipose tissue in a state of diet-induced obesity and IR. In the same study, it was shown that STAT3 signaling of T cells is crucial in the development of inflammation and IR.

This notion is supported in a study on 80 obese adults meeting the IDF 2007 diagnosis criteria for MetS. When comparing concentrations of adipocytokines in the studied group and control group, researchers found that patients with MetS (studied group) had significantly higher levels of proatherogenic adipokines, including IL-6 [174]. In the Study of Inherited Risk of Coronary Atherosclerosis performed on 875 subjects, IL-6 concentrations were found to be 56% higher in subjects with MetS than subjects without [184]. This same conclusion was supported in the Mohammadi et al. [185]. Similarly, in a characteristic rat model of MetS used to determine association of elevated IL-6 levels with the prevalence of MetS and CVD, data showed that IL-6 was significantly associated with HOMA-IR, LDL, TC, TRG, and body weight. Researchers concluded that IL-6 may be used as a representative biomarker in the development of MetS [186]. In another study performed on 68 subjects with newly diagnosed T2D, including 51 of those participants being diagnosed with MetS, data reported that the diabetic patients

with MetS had significantly higher IL-6 concentrations than diabetic patients without MetS [187].

Cardiometabolic Biomarkers of Metabolic Syndrome

Specific cardiometabolic risk factors associated with MetS include total cholesterol (TC) (HDL and LDL), TRG, systolic and diastolic blood pressure, and plasma glucose, insulin, cortisol, and IL-6 concentrations [188, 189]. These biomarkers are used as measurable indicators of the presence of metabolic dysfunction [180, 190]. In dietary intervention studies, selection of relevant biomarkers is important to assess diagnosis and prognosis of MetS, as well as compliance or effect of the nutritional intervention [191, 192].

Cardiometabolic biomarkers of MetS studied extensively in the literature include TC (HDL and LDL) and TRG, whose simultaneous increase is known as atherogenic dyslipidemia [89, 193-195]. Typically, dyslipidemia of individuals with MetS consists of decreased HDL, increased LDL; and therefore, increased TC, as well as increased levels of TRG (hypertriglyceridemia) [196]. While in a state of obesity, metabolism of HDL is impaired, and expression of the LDL receptor is decreased [197]. According to the Centers for Disease Control and Prevention, TC should not exceed 200 mg/dL, LDL cholesterol should not exceed 100, and HDL should be greater than 60 mg/dL. Whereas, an individual with MetS may have TC above 240 mg/dL, LDL cholesterol greater than 160 mg/dL, and HDL less than 40 mg/dL in men and 50 mg/dL in women [198].

Increased levels of TRG affect approximately 15-20% of the adult population, and are associated with obesity, MetS, and T2D [199]. In a survey performed on more than 6,500 U.S.

adults, researchers found that increasing rates of sedentary behavior and obesity are positively correlated with increased mean TRG levels [200]. The Mayo Clinic states that normal levels of TRG do not exceed 150 mg/dL, whereas levels of hypertriglyceridemia vary greatly between 150 mg/dL and 500 mg/dL [201]. A separate study aimed to investigate whether the presence of cardiovascular risk factors, including TRG, can predict eventual development of diabetes. Eight hundred and seventy-two individuals with normal or impaired glucose tolerance were assessed for the onset of T2D over the course of five years. Researchers found that participants with high levels of TRG were at an increased risk of developing T2D [202].

Hypertension in relation to MetS and T2D is also frequently the subject of investigation [203-207]. A metabolically healthy individual should have systolic blood pressure less than 120 mmHg and diastolic blood pressure of less than 80 mmHg [208]. Alternatively, an individual with MetS should often have systolic blood pressure greater than 130 mmHg and diastolic blood pressure greater than 85 mmHg [209]. Abnormal systolic and diastolic blood pressure is associated with serious complications, increased mortality, and increasing costs of healthcare [210]. It is well documented that hypertensive patients are at an increased risk of T2D, and therefore, at an increased risk of MetS [211-213]. Diabetic individuals with chronic hypertension were found to be at a 57% increased risk of CVD event and 72% increase in the risk of all-cause death after adjusting for clinical and demographic covariates [214]. In a meta-analysis of 30 prospective studies, researchers found that each increase in systolic blood pressure of 20 mmHg increased the risk of developing T2D by 77% [215]. The same meta-analysis found that T2D was associated with a 0.67 mmHg increase in systolic blood pressure, while diastolic blood pressure was unaffected [212].

Plasma glucose and insulin concentrations are most always utilized in analysis of MetS as they are easily measurable indicators of potentially impaired insulin sensitivity, a primary component of MetS. Although insulin resistance is not a requirement in all definitions of MetS, approximately 70% of patients diagnosed with MetS have high levels of plasma insulin that fail to appropriately suppress plasma glucose [216]. Another study aiming to evaluate elevated glucose concentrations in patients with MetS or T2D found that impaired fasting plasma glucose was an independent predictor of hospitalizations related to heart failure in individuals at high risk for CVD [217]. Similarly, a non-diabetic population with greater than 20,000 subjects were found to have impaired fasting glucose or impaired glucose tolerance that was associated with heart failure [218]. In a separate study of 1,611 subjects, diabetic outcome was predicted by measuring plasma glucose concentrations at 0, 30, 60, and 120 minutes after oral glucose tolerance testing. A repeat oral glucose tolerance test was performed at a 7-8 year follow up, with WHO criteria used to diagnose T2D and the NCEP (ATP III) used to diagnose MetS. Results suggested that plasma glucose concentrations measured at 60 minutes post oral glucose tolerance test are a strong predictor for risk of T2D [219].

Metabolic Syndrome and Body Composition

Certain body composition markers (e.g. weight, BMI, WHR, etc.) are perhaps the most widely measured and readily available data present in most studies on MetS. Individuals accumulate more adipose tissue in insulin-sensitive locations (skeletal muscle, adipose tissue, and liver), dysfunction of the insulin-sensitive tissues occurs, thus leading to insulin resistance, and therefore put the individual at an increased risk of MetS and T2D [220]. Body composition

measurements such as weight, BMI, and WHR are commonly used to evaluate physical qualification for diagnosis of MetS [45, 221]. Previously, the use of BMI to assess obesity and health risks has been negatively scrutinized in clinical literature, primarily because of its inability to discern fat mass from lean mass. However, in a cross-sectional study on 12,294 adults, researchers found that BMI was the strongest predictor of blood pressure and waist circumference, and adequately predicted fasting glucose, and cholesterol levels [222]. In the study of Dulloo et al. [223], researchers concluded that BMI compared to other body composition measurement methods (MRI, DEXA, etc.) is more practical for large studies and in clinical settings due to lower costs in time and money. In a meta-analysis of lifestyle interventions (physical activity, dietary/nutrition) in MetS patients, waist circumference was identified as the most analyzed parameter (88.9% of trials). Body weight (85.2% of trials), BMI (77.8%), and body fat (55.6%) were also frequently used to diagnose patients with or at risk of MetS [224]. Recently, studies have shown that body fat distribution rather than degree of obesity may contribute more to morbidity and mortality, thereby suggesting waist circumference or WHR to be better predictors of MetS and CVD risk compared to BMI [225, 226]. In a study with 30 obese adult men with MetS, researchers found that a decrease in adipose tissue may help to reverse MetS in men with obesity and MetS [227]. Another study found similar results in that body fat percentage correlates with risk factors of CVD and MetS for both men and women [228].

Current Treatments and Interventions

Currently, there are two primary approaches used to treat and manage MetS: pharmacological and lifestyle (e.g. physical activity, nutrition/dietary intake) modification [11].

The first category of treatment methods for MetS is medication. Oftentimes, individuals with MetS are prescribed different medications to treat the multiple components of the condition [229]. In fact, it has been suggested that each risk factor of MetS is considered a possible primary drug target for treatment of MetS [230]. Examples of typical pharmacologic intervention for the treatment of MetS include insulin-sensitizing agents (metformin, thiazolidinediones), statins, and fibrates [231, 232]. Metformin is a popular insulin-sensitizing drug and is currently the most commonly prescribed drug in the world to treat T2D [233, 234]. As well, Metformin is considered the most effective drug to control blood glucose levels and decrease the risk of T2D in individuals with MetS [235]. Statins are prescribed to lower cholesterol levels. In a randomized placebo control trial, Rosuvastatin was shown to have the highest efficacy in decreasing LDL cholesterol, while Atorvastatin was shown to improve hepatic insulin sensitivity in T2D patients [236]. However, it has also been shown that Atorvastatin increased the risk of T2D and induced myopathy, and another statin drug, Simvastatin, increased T2D risk and blood glucose concentrations [237, 238]. One study states that statin drugs are a good option when aiming to lower LDL cholesterol, whereas fibrates are more beneficial for increasing HDL and managing hypertriglyceridemia [239]. Antihypertensive drugs include angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs). ACE inhibitors result in relaxation of the blood vessels, while ARBs cause vasodilation; together, these drugs are used to regulate blood pressure [231]. It is well documented that reduction of blood pressure has benefits in reducing cardiovascular risk in patient with T2D [240-242].

The second category of treatment methods for MetS is lifestyle modification. Lifestyle modification can consist of either implementation of more physical activity or dietary/nutritional intervention. Physical inactivity is an important risk factor for non-communicable diseases, such as CVD and MetS [243]. The effect of physical activity on cardiometabolic biomarkers in relation to MetS has been studied extensively in the literature as a potential treatment for MetS. It is well-established that physical activity has positive effects on cardiometabolic health [244]. One study even suggests that sedentary time could be considered an independent risk factor of CVD [245]. Studies show that regular physical activity is associated with significant improvement of blood glucose levels, weight loss, and reduction in waist circumference, as well as prevention of the onset of T2D [246-248]. In a study of thirty-two subjects with MetS, researchers aimed to investigate whether exercise intensity had differing effects on markers of MetS. When comparing aerobic-interval training to continuous moderate exercise, aerobic interval training was shown to be more beneficial for improving aerobic capacity and biomarkers of MetS [249]. Similarly, in a study on 262 T2D individuals comparing aerobic training, resistance training, and aerobic plus resistance training, researchers found that aerobic and aerobic plus resistance training significantly improved risk and prevalence of MetS in T2D individuals [250]. Similar results in relation to the benefits of physical activity on cardiometabolic risk factors associated with MetS can be found in the study of Ostman et al., and elsewhere [251-254].

Lifestyle modification, especially in the realm of dietary behaviors, is considered the primary therapeutic strategy for treatment and management of MetS [255]. Many different types of dietary interventions and their impact on MetS have been studied in the literature

including time restricted feeding and intermittent fasting, as well as the paleolithic, ketogenic, Mediterranean, and high protein diets. Recently, time-restricted feeding has been studied extensively in the literature as an effective nutritional strategy for improving markers of MetS and T2D [256-258]. A meta-analysis evaluating the efficacy of time-restricted feeding methods in obese and overweight subjects found that subjects following a time-restricted feeding regimen had significantly reduced weight and fat mass. As well, time-restricted feeding had favorable effects on blood pressure, fasting glucose concentrations, and cholesterol levels [259]. A randomized clinical control trial performed on 70 subjects with MetS compared intermittent energy restriction with continuous energy restriction and found that both methods improved markers of metabolic syndrome associated with weight loss [260]. Alternatively, a separate non-randomized controlled clinical trial on thirty-two obese women found that after three months following a 16 hour fasting regimen that time-restricted feeding successfully reduced body weight, but did not affect biomarkers of MetS [261]. Only a few studies have been done to assess the effects of a paleolithic diet on individuals with MetS. Researchers conducted a systematic review of four randomized control trials involving 159 subjects with one or more components of MetS who received a paleolithic dietary intervention. Data analysis concluded that a paleolithic-style diet showed better short-term improvements in features of MetS when compared to control interventions [262-266]. Researchers have also considered the use of a ketogenic diet in the management of cardiometabolic markers of MetS [267-272]. Studies show that following a ketogenic diet will result in decreased TRG, reduced total cholesterol, increased HDL, and decreased size and volume of LDL cholesterol [273-276]. Another widely researched dietary treatment in relation to MetS is the Mediterranean diet. In

fact, the Mediterranean diet is one of the most widely researched dietary patterns in the world, with a substantial amount of evidence to support its role in improving cardiovascular risk factors, and pose potential benefits for incidence of T2D and MetS [277-283]. In a randomized single-blind trial, 180 patients with MetS received either a Mediterranean-style (intervention) or a prudent (control; carbohydrates 50-60%, proteins 15-20%, total fat <30%) dietary intervention. After a two year follow up, only forty participants in the intervention group had features of MetS, compared to seventy in the control group, leading researchers to conclude that a Mediterranean-style diet may be an effective method for managing and treating MetS [284]. However, a 21-day randomized controlled inpatient crossover feeding trial of 20 obese women with IR suggested that when compared to a HPD, the Mediterranean diet resulted in poorer control of IR and glycemic variability [285]. The remainder of this review will focus on the use of higher protein diets (HPD) as a treatment method in the prevention and management of MetS. Many researchers have investigated the effects of HPD on body composition and cardiometabolic biomarkers of MetS. Studies have shown that HPD promote weight loss, improve glucose homeostasis, increase energy expenditure, and increase fat oxidation in the adult population [286, 287].

Dietary Protein and Cardiometabolic Health

Recently, HPD have been the subject of much investigation [12-22]. Research has shown that consumption of HPD (20-35% of macronutrient intake) have resulted in reduced body weight and fat mass while preserving more lean mass and increasing energy expenditure when compared to a standard protein diet (SPD) (12–18% of macronutrient intake) [25-30]. This is especially important, as maintaining fullness and fat-free mass is essential to maintaining

weight-loss effects [288]. It is acknowledged that HPD may be potentially helpful at promoting and maintaining weight loss, especially in a short-term setting due to the increased thermogenic effect of protein [289-292]. In a six-month randomized dietary intervention, fifty participants were prescribed a HPD (25% of macronutrient intake), high-carbohydrate diet (protein as 12% of total macronutrient intake), or control group (fat intake as 30% of total macronutrient intake). At the conclusion of the clinical trial, participants in the HPD group had more significant reductions in body weight and fat mass compared to other treatments groups [293]. In a meta-analysis of 24 randomized control trials involving 1,063 subjects, participants consuming a HPD (27-35% of macronutrient intake) lost significantly more body weight, fat mass, and TRG when compared to the SPD group. The HPD group also conserved more fat-free mass and resting energy expenditure [25]. Further studies confirming improvement in body composition under conditions of a HPD can be explained in detail elsewhere [294-296]. A randomized control trial on 105 subjects with MetS compared a HPD (providing 1.34 g/kg body weight/day) or a SPD (providing 0.8 g/kg body weight/day) over the course of six months. Results showed no significant difference in weight loss and biomarkers of MetS when examining the overall group, however when accounting for adherence to each intervention, participants with high adherence in the HPD group showed significantly more weight loss when compared to participants with high adherence in the SPD group [297]. In the review of Te Morenga and Mann, data showed that higher intake of protein (25-30% of macronutrient intake) are useful for weight loss/maintenance and are potentially beneficial as a treatment method for MetS [298]. In a dietary intervention involving forty-three overweight and obese men, subjects were prescribed either a HPD (25% of macronutrient intake) or SPD (15% of

macronutrient intake). Measurements of weight, body composition, indices of metabolic syndrome, and resting energy expenditure were recorded over the course of twelve weeks. Researchers found that consumption of a HPD aided in the preservation of more muscle mass while experiencing weight loss compared to a standard protein diet [41]. One systematic review and meta-analysis evaluated the effects of high-protein, low fat diets compared to standard-protein, low-fat diets on weight loss, body composition, resting energy expenditure, satiety and appetite, and cardiometabolic biomarkers. Data showed that an isocalorically prescribed high-protein, low-fat diet showed notable benefits for weight loss, fat loss, and reduction in TRG, while mitigating reductions in resting energy expenditure and fat-free mass [25]. Similarly, in a six-month randomized trial analyzing eighty obese women (BMI of 37.7 ± 3.39 kg/m²) data showed that an energy-restricted diet containing 35% protein had a greater impact on cardiometabolic profile than energy-restricted diets containing 20% and 27% protein. However, the same study showed no significant difference in overall weight loss between groups [299]. One systematic review and meta-analysis concluded that HPD did not provide benefits nor detrimental effects on cardiometabolic biomarkers of MetS. Interestingly, two separate studies evaluating the effect of HPD on markers of MetS in Southeast Asian Indians and Koreans found that increased protein to carbohydrate ratio was associated with increased risk of T2D [300, 301]. Additional studies evaluating the effects of a HPD on cardiometabolic risk factors are described in detail elsewhere [302-308].

Dietary Protein and Appetite

Overnutrition is the main driver of obesity-related cardiometabolic dysfunction, therefore, finding an intervention to aid in appetite control is essential [23, 309]. Studies show

that short-term consumption of HPD results in appetite suppression, through decreased levels of orexigenic hormones such as ghrelin, and increased levels of anorexigenic hormones such as cholecystokinin (CCK) and GLP-1 [23]. One study aimed to compare the effects of ingestion of a high-protein test meal (short-term) and habitual HPD consumption (long-term). Results of this study demonstrated that the short-term satiating effect of protein varies inversely with long-term satiating effect [310]. A separate study compared postprandial effect of a standard protein meal (14% of macronutrient intake), a medium-high protein meal (25% of macronutrient intake), and a high-protein meal (50% of macronutrient intake) on twenty-five overweight men. Results showed that increased intake of protein (25% of 50%) had significantly greater effects on satiety through increased levels of GLP-1, peptide YY (PYY), and glucagon when compared to a standard protein meal [311]. A 2020 meta-analysis aiming to investigate the effects of a high-protein diet on appetite sensations in individuals with overweight and obesity evaluated ten different studies involving 1079 subjects. Results of the data analysis indicated that participants consuming a HPD experienced improved feelings of satiety as a result of the dietary intervention [312]. In a study on 156 obese adolescents, participants assigned to consume a higher protein breakfast (egg) experienced greater levels of PYY and GLP-1, resulting in decreased lunchtime food intake and body weight when compared to a low-protein breakfast (steamed bread) over the course of four hours tested at baseline and three months [313]. Similar results were found in the study of Leidy et al., which concluded that a consumption of a high protein breakfast resulted in improved satiety and reductions in daily food intake [314]. In a meta-analysis reviewing habitual HPD consumption in various clinical trials, researchers outlined how HPD result in increased satiety through elevated levels of

anorexigenic hormones, decreased levels of orexigenic hormones, elevated plasma amino acid levels, increased hepatic gluconeogenesis, and increased ketogenesis from the higher protein intake and increased energy expenditure through increased diet-induced thermogenesis [24]. A 2021 study on twenty-four obese, prediabetic subjects consuming a HPD or SPD measured GLP-1, GIP, Ghrelin, BNP, insulin and glucose at baseline and 6 months. Results showed that subjects consuming the HPD had decreased concentrations of the orexigenic hormone, ghrelin, therefore indicating that habitual consumption of a HPD may reduce hunger more effectively than a SPD [315]. In a separate study involving nineteen subjects, researchers prescribed a weight-maintaining diet (15% protein, 35% fat, and 50% carbohydrate) for 2 weeks, an isocaloric diet (30% protein, 20% fat, and 50% carbohydrate) for 2 weeks, and an ad libitum diet (30% protein, 20% fat, and 50% carbohydrate) for 12 weeks. At the conclusion of the study, satiety was notably increased in the diets containing 30% protein, resulting in decreased ad libitum food intake and significant weight loss [316].

Gaps in the Literature

Obesity-related cardiometabolic dysfunction, particularly MetS, is a public health concern with approximately 30% of the U.S. population qualifying for a diagnosis. Currently, treatment methods consist of medications, increase in physical activity, or dietary intervention. There has been a robust amount of research conducted on the topic of HPD and its effect on cardiometabolic biomarkers in a state of weight loss. However, very few studies have been performed to investigate the role of the carbohydrate source in conjunction with a HPD in a state of weight maintenance and its effects on cardiometabolic biomarkers in adults at risk for MetS.

Therefore, the overall goal of this thesis was to determine the role of the carbohydrate source with a HPD on cardiometabolic biomarkers in adults at risk for MetS.

The objectives of this study are as follows:

Objective 1: Determine the short-term effects of a carbohydrate source with a HPD on biomarkers in adults at risk for MetS.

Objective 2: Determine the long-term effect of a carbohydrate source with a HPD on cardiometabolic biomarkers in adults at risk for MetS.

We hypothesized:

Hypothesis 1: HPD containing white potatoes will improve appetite response in adults at risk for MetS.

Hypothesis 2: HPD containing white potatoes will improve cardiometabolic biomarkers in adults at risk for MetS.

Chapter One Tables

Table 1. Definitions of Metabolic Syndrome

| | World Health Organization 1999 | International Diabetes Federation 2005 | National Cholesterol Education Program (Adult Treatment Panel III) 2005 |
|---|---|--|---|
| Required | Insulin resistance* (IGT, IFG, T2D or other evidence of IR) | Central obesity (waist circumference§): ≥ 94 cm (M), ≥ 80 cm (F) | None |
| Criteria | Insulin resistance or diabetes, plus two of the five criteria below | Obesity, plus two of the four criteria below | Any three of the five criteria below |
| Obesity | Waist/hip ratio: > 0.90 (M), > 0.85 (F); or BMI > 30 kg/m ² | Central obesity already required | Waist circumference: > 40 inches (M), > 35 inches (F) |
| Hyperglycemia | Insulin resistance already required | Fasting glucose ≥ 100 mg/d | Fasting glucose ≥ 100 mg/dl or Rx |
| Dyslipidemia | TG ≥ 150 mg/dl or HDL: < 35 mg/dl (M), < 39 mg/dl (F) | TG ≥ 150 mg/dl or Rx | TG ≥ 150 mg/dl or Rx |
| Dyslipidemia (second, separate criteria) | | HDL cholesterol: < 40 mg/dl (M), < 50 mg/dl (F); or Rx | HDL cholesterol: < 40 mg/dl (M), < 50 mg/dl (F); or Rx |
| Hypertension | ≥ 140/90 mmHg | > 130 mmHg systolic or > 85mmHg diastolic or Rx | > 130 mmHg systolic or > 85mmHg diastolic or Rx |
| Other criteria | Microalbuminuria† | | |

*IGT, impaired glucose tolerance; IFG, impaired fasting glucose; T2D, type 2 diabetes; IR, insulin resistance; other evidence includes euglycemic clamp studies.

§Criteria for central obesity (waist circumference) are specific for each population; values given are for European men and women.

Rx, pharmacologic treatment

†Urinary albumin excretion of 20 µg/min or albumin-to-creatinine ratio of 30 mg/g.

Chapter 2

Carbohydrate Source Within Higher Protein Diets Does Not Affect Appetite Response or Cardiometabolic Biomarkers in Adults at Risk for Metabolic Syndrome

Abstract

Background. As prevalence of obesity increases so does the incidence of obesity-related metabolic diseases such as the metabolic syndrome (MetS). MetS affects approximately 30% of U.S. adults and is associated with a 3-5-fold increased risk of T2D. Studies have shown that short-term consumption of HPD results in appetite suppression, through decreased levels of orexigenic hormones and increased level of anorexigenic hormones.

Justification. Research has suggested that inclusion of white potatoes in a mixed meal will improve postprandial markers of appetite. The role of the carbohydrate source consumed with a HPD and its impact on MetS has not been researched and is therefore a gap in the literature.

Objective and Hypothesis. Determine the short-term effects of carbohydrate source with HPD on markers of MetS. HPD containing white potatoes will improve markers of MetS in individuals at risk for MetS.

Materials and Methods. In this 240-minute acute randomized, controlled study (n=23; 15 females and 8 males; age 35.7 ± 6.0 y, weight 100.65 ± 5.44 kg, BMI 36.4 ± 2.5 kg/m²), participants consumed a higher protein test breakfast containing white potatoes or a control carbohydrate (white rice) and were evaluated for response of appetite, palatability, and fasting glucose and insulin. At each of 0, 30, 60, 120, 180, 240 minutes, a 10 ml whole blood sample

was collected, and a VAS on subjective appetite was completed. At minute fifteen, a VAS on subjective palatability of the test breakfast was collected.

Results. There were no significant differences in markers of appetite, palatability, or cardiometabolic response between treatment groups.

Conclusions. Consumption of a higher protein test breakfast containing white potatoes compared to a higher protein test breakfast containing a control carbohydrate (white rice) did not show overall improvement in markers of appetite, palatability, and cardiometabolic response in adults at risk for MetS.

Introduction

Obesity has become a significant health problem in the United States and across the globe [1]. Recent findings suggest that approximately 50% of U.S. adults will have obesity and 25% will have severe obesity (body mass index (BMI) > 40 kg/m²) by the year 2030 [2]. As rates of obesity increase, so too does prevalence obesity-related diseases, such as the metabolic syndrome. Metabolic syndrome (MetS) is a clustering of cardiometabolic risk factors including insulin resistance (IR), visceral adiposity (VA), atherogenic dyslipidemia (AD), and endothelial dysfunction (ED) [8]. Each risk factor has its own detrimental effects, however, when these risk factors are grouped together they can have an even greater impact [9]. Globally, prevalence of MetS has reached 31%, and is associated with a 1.5-fold increase in the risk of all-cause mortality [31]. If left untreated, the cardiometabolic risk factors of MetS aid in the development of cardiovascular disease (CVD) and type 2 diabetes (T2D) [10].

Overnutrition is the main driver of obesity-related cardiometabolic dysfunction, therefore, finding an intervention to aid in appetite control is essential [23, 309]. Recently, higher protein diets (HPD) have been the subject of much investigation [12-22]. The daily recommended protein intake for adults is 0.80 g/kg body weight/day, (10–15% of macronutrient intake) [35]. However, researchers suggest that the daily recommendation for protein intake should be increased to 20-35% as the benefits of protein intake beyond the recommendations are well-established [33-35]. Studies have shown that short-term consumption of HPD results in appetite suppression [23, 24]. A 2020 meta-analysis aiming to investigate the effects of a high-protein diet on appetite sensations in individuals with overweight and obesity evaluated ten different studies involving 1079 subjects. Results of the data analysis indicated that participants consuming a HPD experienced improved feelings of satiety as a result of the dietary intervention [312]. In a study on 156 obese adolescents, participants assigned to consume a higher protein breakfast (egg) experienced greater levels of PYY and GLP-1, resulting in decreased lunchtime food intake and body weight when compared to a low-protein breakfast (steamed bread) over the course of four hours tested at baseline and three months [313]. Similar results were found in the study of Leidy et al., which concluded that a consumption of a high protein breakfast resulted in improved satiety and reductions in daily food intake [314]. In a meta-analysis reviewing habitual HPD consumption in various clinical trials, researchers outlined how HPD result in increased satiety through elevated levels of anorexigenic hormones, decreased levels of orexigenic hormones, elevated plasma amino acid levels, increased hepatic gluconeogenesis, and increased ketogenesis from the higher protein intake and increased energy expenditure through increased diet-induced thermogenesis [24]

There has been a large amount of research done on the topic of HPD and its effect on cardiometabolic biomarkers in adults with MetS. However, very few studies have been performed to investigate the role of the carbohydrate source in conjunction with a HPD and its effects on cardiometabolic biomarkers in adults at risk for MetS.

White potatoes are often denigrated in nutrition circles due to their frequent association with high fat diets. Typically, consumers believe that white potatoes are higher in fat and calories than other carbohydrate sources such as rice or pasta. However, white potatoes have a similar nutrient composition to that of white rice, though white potatoes have greater amount of certain vitamins and minerals [317]. The white potato is indeed an excellent source of key nutrients such as carbohydrate, dietary fiber, vitamin B6, vitamin C, and potassium [317, 318]. Research has suggested that inclusion of white potatoes in a mixed meal will improve postprandial markers of appetite [319-322]. One study evaluated consumption of potatoes, rice, or pasta with 150 g of pork steak on participants' (n=11) levels of hunger/satiety, food intake, plasma insulin, glucose, and ghrelin concentrations. Results indicated that consumption of satiating amounts of potatoes consumed with meat (high protein) were associated with increased satiety (lower energy intake) following the test meal. Additionally, consumption of satiating amounts of potatoes consumed with meat (high protein) were associated with lower postprandial insulin concentrations when compared to the rice- or pasta-consuming groups [323].

The objective of this study was to determine the short-term effects of a higher protein test breakfast containing white potatoes or a control carbohydrate (white rice) on biomarkers in adults at risk for MetS.

Materials and Methods

Participants and ethical approval. From May 2019 to August 2022, adult male and female participants between the ages of 25 and 50 years old were recruited to participate in this acute randomized, controlled study (n=23; 15 females and 8 males; age 35.7 ± 6.0 y, weight 100.65 ± 5.44 kg, BMI 36.4 ± 2.5 kg/m²). There were three phases of the recruitment plan. In *Phase 1* of the recruitment, participants were recruited from the Northwest Arkansas area through advertisements posted in the local university daily newsletter (University of Arkansas Newswire), and through flyers posted throughout the Northwest Arkansas community, social media, and word-of mouth. *Phase 2* of recruitment involved a screening questionnaire administered by phone. Interested participants reached out via email and were scheduled for an initial phone screening. A total of 225 individuals completed the phone screening and 169 individuals were excluded as they did not meet the enrollment criteria. Individuals who had food allergies or dietary restrictions (e.g., vegetarian, Halal/Kosher, low-carbohydrate, gluten free), were actively trying to lose weight, had lost greater than five percent of their body weight over the past three months, were taking prescription medications, had a body mass index (BMI) less than 25, had any pre-existing cardiometabolic conditions (congestive heart failure or cardiomyopathy, etc.), had chronic mental health issues (e.g., depression, anxiety, etc.), or were uncomfortable/had a fear of needles were excluded from participating in this study. *Phase 3* was the final stage of recruitment which included an in-person clinical. Participants who met the initial phone screening criteria underwent an in-person screening at The Center for Human Nutrition (University of Arkansas, Fayetteville, AR) to determine physical eligibility. A total of 56 individuals qualified for the in-person screening. Fourteen individuals failed to confirm the

appointment or were absent at their scheduled clinical screening time. The 32 individuals who attended were screened for two or more characteristics of MetS (body mass index (BMI) >25, abdominal obesity (waist-to-hip ratio (WHR) ≥ 0.90 cm in men and ≥ 0.85 cm in women), triglyceride (TRG) level > 150 mg/dL, HDL cholesterol < 40 mg/dL in men and 50 mg/dL in women, systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg, and/or fasting glucose > 100 mg/dL). Out of the 32 participants who were clinically screened, a total of 26 participants were recruited and allocated into two treatment groups. Written consent was obtained from all participants prior to beginning the study. Twenty-three men and women were analyzed for appetite response and twenty participants were analyzed for cardiometabolic response at the conclusion of the study. Three participants dropped out of the intervention for reasons including failed blood collection and religious considerations. Refer to **Figure 1** for flow diagram of the recruitment and participation process. Ethical approval for the study protocol was obtained from the Office of Research Compliance Institutional Review Board of the University of Arkansas (Fayetteville, AR). This trial was registered at clinicaltrials.gov (NCT03935048).

Study design. Refer to **Figure 2** for study design. Participants were randomized to one of two treatments groups: 1) high protein breakfast containing white potatoes (HPWP; n=12, 9 females and 3 males, age 39.9 ± 11.9 y, BMI 38.2 ± 21.7 kg/m²) or 2) high protein breakfast with control carbohydrate (white rice) (HPCC; n=11, 6 females and 5 males, age 31.5 ± 5.5 y, BMI 34.7 ± 6.0 kg/m²). Refer to **Table 2** for participant characteristics. On the study day, participants arrived at the Center for Human Nutrition at the University of Arkansas after an overnight fast of 8-10

hours for data collection. Upon arrival, participants were screened for COVID-19 and anthropometric measurements were recorded. An intravenous catheter was inserted into an antecubital vein and a fasting whole blood sample was collected by a licensed phlebotomy technician. Fasting measurements of self-reported appetite via the visual analogue scale (VAS) were recorded. At minute zero, each participant received a pre-prepared higher protein test breakfast per their randomized dietary assignment. Participants were required to finish the higher protein test breakfast within 15 minutes. At minute 15, a VAS on subjective appetite and palatability of the test breakfast were collected. At each of 30, 60, 120, 180, 240 minutes, a 10 ml whole blood sample was collected in EDTA vacutainer tubes, and a VAS on subjective appetite was completed.

Dietary intervention. In dietary treatment 1, high protein diet containing white potatoes (HPWP), participants consumed a higher protein test breakfast containing: 75 grams white potatoes, 2 large eggs (Eggland's Best), 23 grams sausage crumble (Jimmy Dean), 2 tablespoons skim milk, and 30 grams cheese (Kraft – mild cheddar). In dietary treatment 2, high protein diet without potatoes (HPCC), participants consumed a higher protein test breakfast containing 54 grams white rice, 2 large eggs (Eggland's Best), 23 grams sausage crumble (Jimmy Dean), 2 tablespoons skim milk, and 30 grams cheese (Kraft – mild cheddar). All test breakfasts were isocaloric, volume matched, and macronutrient matched. Refer to **Table 3** for nutrient composition of the test breakfasts. Palatability of the test breakfasts was measured using a visual analogue scale.

Anthropometric measurements. Anthropometrics measurements were recorded at the start of the study visit. Body height and weight measurements were taken without shoes or extra materials on the subject. Body weight was measured to the nearest 0.05 kg using calibrated balance scales (Detecto, St. Louis, MO). Body height was measured to the nearest 0.1 cm in the free-standing position using a stadiometer (Detecto, St. Louis, MO). Using a standard measuring tape, waist-to-hip ratio (WHR) was calculated with waist circumference taken at the top of the iliac crest and hip circumference taken around the widest portion of the buttocks.

Appetite Response. To assess postprandial appetite and palatability response, a traditional 100 mm Visual Analogue Scale (VAS) with opposing anchors (i.e., “very hungry” or “not at all hungry”) was used. The VAS scale is used to measure a characteristic or attitude across a continuum, rather than based on discrete jumps [324]. Appetite was measured at 0, 30, 60, 90, 120, 180, and 240 minutes using a series of 7 questions. Participants were asked to indicate how hungry, how full, how strong their desire to eat, how much food they could eat, desire for something salty, desire for something sweet, and their desire for a snack. Palatability was measured at the conclusion of the test breakfast (15 minutes). An “X” was placed on the 100 mm VAS scale where the subject thought most accurately represented their subjective levels of appetite or palatability. To evaluate appetite response in addition to VAS analysis, concentrations of plasma glucose and insulin were measured at 0, 30, 60, 120, 180, and 240 minutes.

Statistical analysis. Summary statistics were calculated for all data and data are expressed as mean \pm standard deviation. All data was analyzed using the statistical software GraphPad Prism version 9.0. All statistical tests were two sided with P-values \leq 0.05 used to indicate statistical significance. Two-way ANOVA was used to determine differences in cardiometabolic biomarkers between dietary interventions.

Results

Participant characteristics. The demographics and physical characteristics of the participants who completed the study are presented in **Table 1** and **Table 2**, respectively. The HPCC group and HPWP group had a mean age of 31.5 ± 5.5 y and 40.0 ± 11.7 y respectively. There were no significant differences in age, weight, height, BMI, or WHR between groups.

Cardiometabolic biomarkers. Cardiometabolic biomarkers were analyzed for twelve participants in the HPWP group and eight participants in the HPCC group. Three participants in the HPCC group were not analyzed for cardiometabolic biomarkers due to failed blood collection at certain timepoints. Postprandial plasma insulin and glucose results are presented in **Table 4**. Additionally, postprandial plasma glucose and insulin results are graphically presented in **Figure 3** and **Figure 4**, respectively. There was a significant effect of time ($P < 0.0001$) on plasma insulin and glucose concentrations for both HPWP and HPCC groups. However, there was no effect of diet or time x diet on plasma insulin and glucose concentrations between groups.

Appetite response and palatability. Appetite response and palatability of the higher protein test breakfasts were analyzed for twelve participants in the HPWP group and eleven participants in the HPCC group. Appetite and palatability results are presented in **Figures 5 and 6**. There was a significant effect of time ($P < 0.0001$) on hunger, fullness, desire to eat, how much one could eat, and desire for a snack for both HPWP and HPCC groups. There was no effect of time x diet for hunger, fullness, desire to eat, how much one could eat, desire for something salty, desire for something sweet, or desire for a snack in either group. There was also no significant difference between the HPWP and HPCC groups for palatability of the higher protein test breakfasts.

Discussion

To our knowledge, this is the first study to examine the role of the carbohydrate source with a higher protein test meal on markers of metabolic syndrome in adults at risk for MetS. The present study tested the hypothesis that HPD containing white potatoes will improve postprandial markers of MetS in adults at risk for MetS. Our results indicate that a higher protein test meal containing white potatoes does not lead to significant changes in appetite, palatability, or plasma biomarkers within 240 minutes of test breakfast consumption when compared to a higher protein test breakfast containing white rice. Collectively, this data suggests that in adults at risk of MetS, consumption of higher-protein meal containing white potatoes will not negatively impact markers of MetS. In addition, carbohydrate source within a higher-protein meal does not alter appetite response.

In the current study, there was no effect of carbohydrate source on postprandial appetite response. These findings align with the results of a study evaluating levels of satiation and satiety following consumption of carbohydrate-rich side dishes in twelve healthy-weight individuals. No significant differences were found in levels of hunger and fullness between test dishes (baked white potato, mashed white potato, brown rice, spaghetti, or white bread) [325].

Research has suggested that inclusion of white potatoes in a mixed meal will improve postprandial markers of appetite [319-322]. A separate study evaluated consumption of potatoes, rice, or pasta with 150 g of pork steak on participants' (n=11) levels of hunger/satiety, food intake, plasma insulin, glucose, and ghrelin concentrations. Results indicated that consumption of satiating amounts of potatoes consumed with meat (high protein) were associated with increased satiety (lower energy intake) following the test meal. Additionally, consumption of satiating amounts of potatoes consumed with meat (high protein) were associated with lower postprandial insulin concentrations when compared to the rice- or pasta-consuming groups [323]. In the current study, we hypothesized there would be a significant change in postprandial insulin and glucose concentrations over time for both the HPWP and HPCC groups, as consumption of a meal containing carbohydrates will cause elevation of blood sugar levels, thus leading to increased insulin secretion [326]. The HPWP group showed greater overall insulin response following consumption of the test breakfast compared to the HPCC group., although the difference was not significant. Peak insulin response was reached at 30 minutes and was greater ($110.1 \pm 59.1 \mu\text{IU/mL}$) for the HPWP group, whereas the HPCC group did not reach peak insulin response until 60 minutes following test breakfast consumption and was lower ($86.0 \pm 43.1 \mu\text{IU/mL}$). These results align with those of a previous study, which

indicated that consumption of white potatoes as a mixed meal resulted in a greater postprandial insulin response [327].

Postprandial responses of plasma glucose concentrations were not significantly different between groups over time. These results align with a previous randomized, cross-over study involving 24 males and females with T2D in which researchers determined that no differences were detected between trials in postprandial glucose concentrations after consumption of a test meal containing white potatoes (boiled, roasted, or boiled and cooled for 24), or basmati rice [328]. However, participants' T2D in the aforementioned study were metformin controlled in some cases, whereas prescription medications would have excluded a participant from the current study.

To our knowledge, this is the first short-term study to examine the role of the carbohydrate source with a higher protein test breakfast on markers of metabolic syndrome in adults at risk for MetS. However, there are several limitations to this study. Although recruitment aimed to balance gender between treatment groups, both treatment groups primarily consisted of females (HPWP; 9 females and 3 males, HPCC; 7 females and 4 males). The sample size of this study was small (n=23). Ninety percent of individuals who were screened to participate in this study did not meet the criteria for inclusion. Therefore, this study should be considered a pilot study. Both groups were primarily Caucasian (HPWP; 11, HPCC; 6), however the HPCC group was more diverse than the HPWP group. The HPWP group had at least one participant in each of Asian, African American, Caucasian, and Hispanic categories, whereas the HPCC group was less diverse with only one non-Caucasian participant (Asian). Finally, beyond the test breakfast, no other form of dietary assessment was performed. This could have

been a contributing factor in the lack of measured significant effects between the dietary treatment groups. Therefore, future research should focus on whether consumption of a higher protein test breakfast containing white potatoes has similar effects on ad libitum food intake following test breakfast consumption compared to a higher protein test breakfast containing a control carbohydrate (white rice).

Conclusion

In conclusion, there was no difference in postprandial appetite response for higher protein test meal containing white potatoes compared to a higher protein test meal containing a control carbohydrate (white rice) in adults at risk for MetS.

Chapter Two Figures

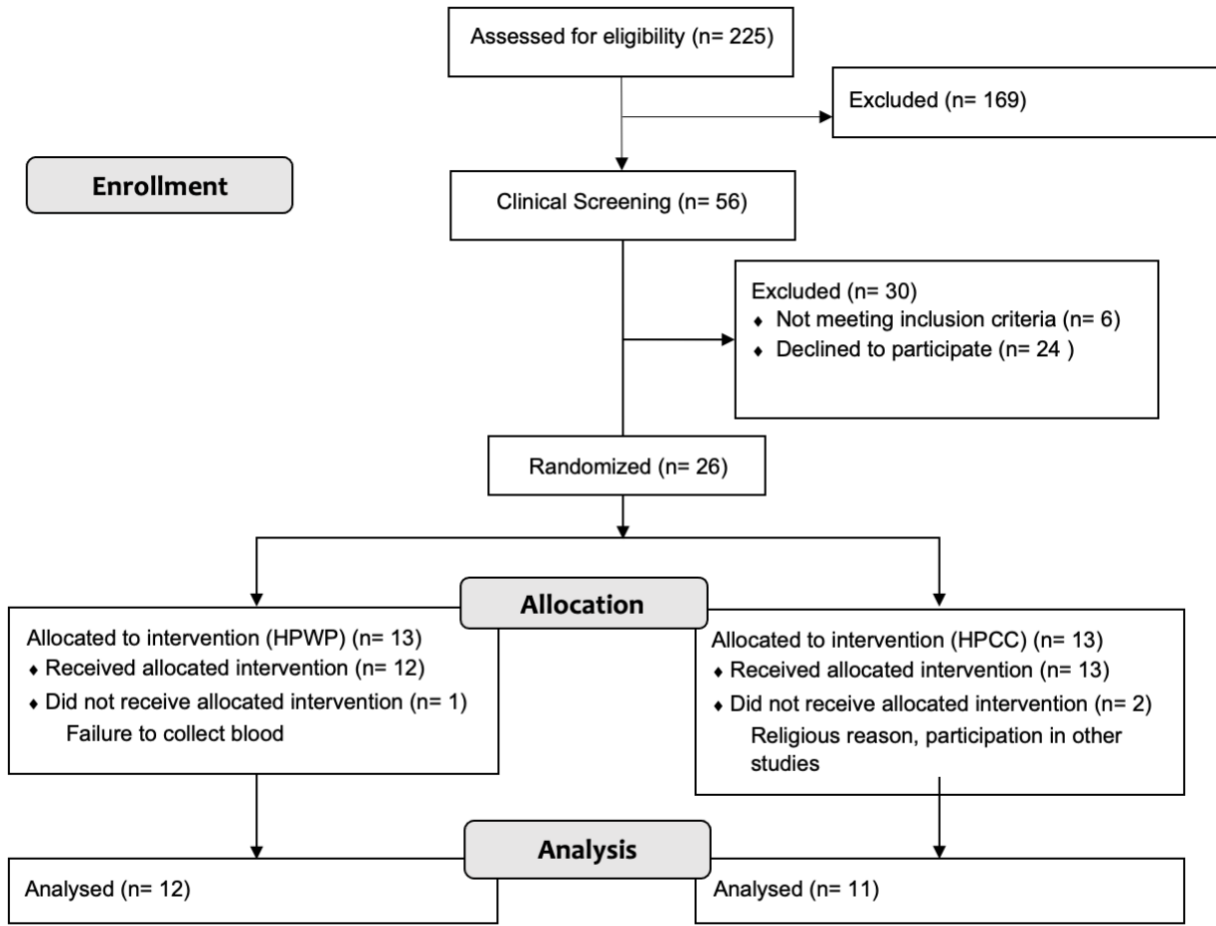


Figure 1. Flow chart showing number of subjects recruited and their attrition patterns during the dietary intervention study. HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=11. Reason for subject withdrawal were as follows: failure to collect blood at baseline (1), participation in Ramadan fasting (1), and unexpected participation in other studies (1).

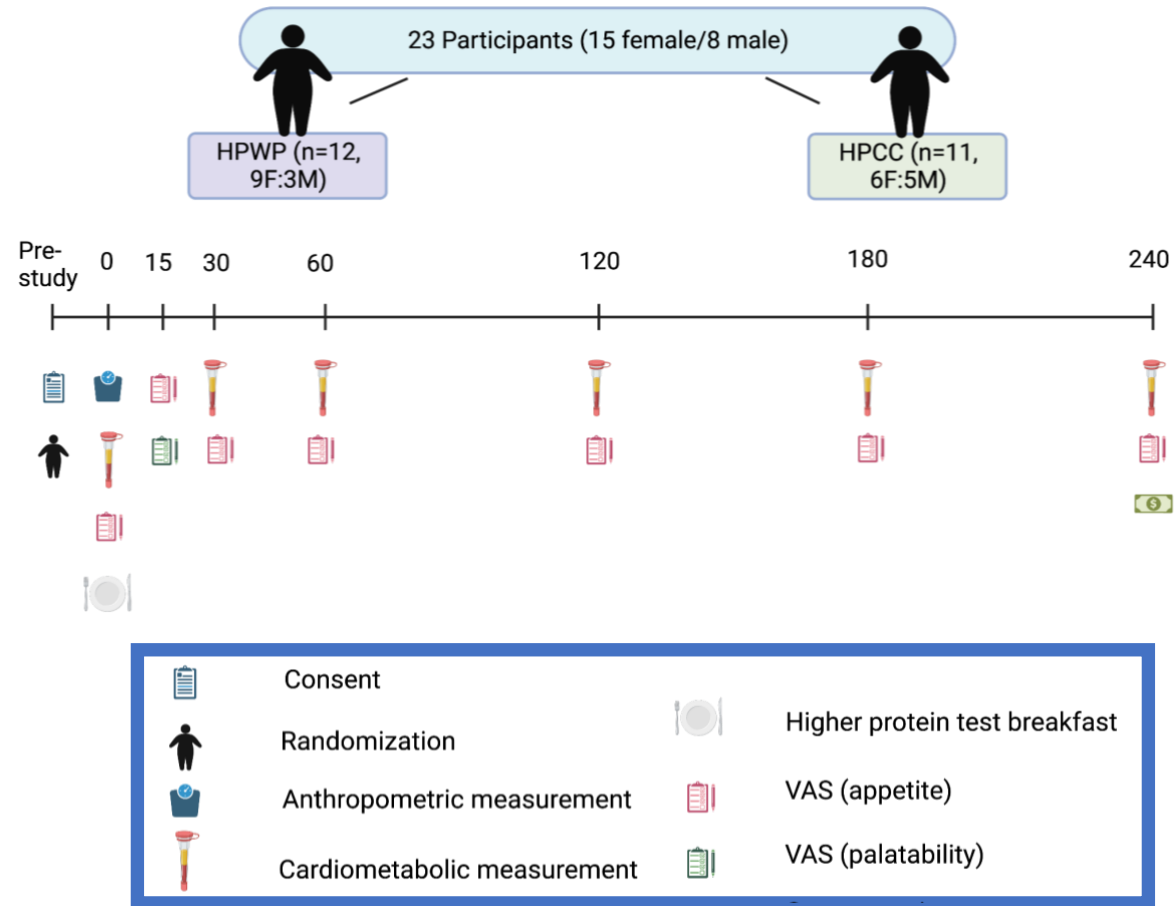


Figure 2. Schematic representation of study design.

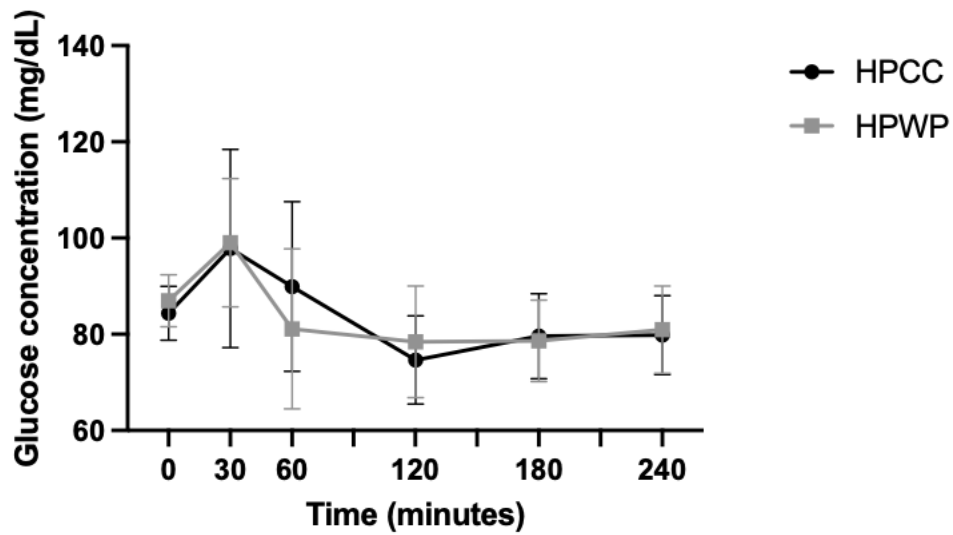


Figure 3. Postprandial glucose response following ingestion of either higher protein test breakfast containing white potatoes or higher protein test breakfast containing a control carbohydrate (white rice). HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=8.

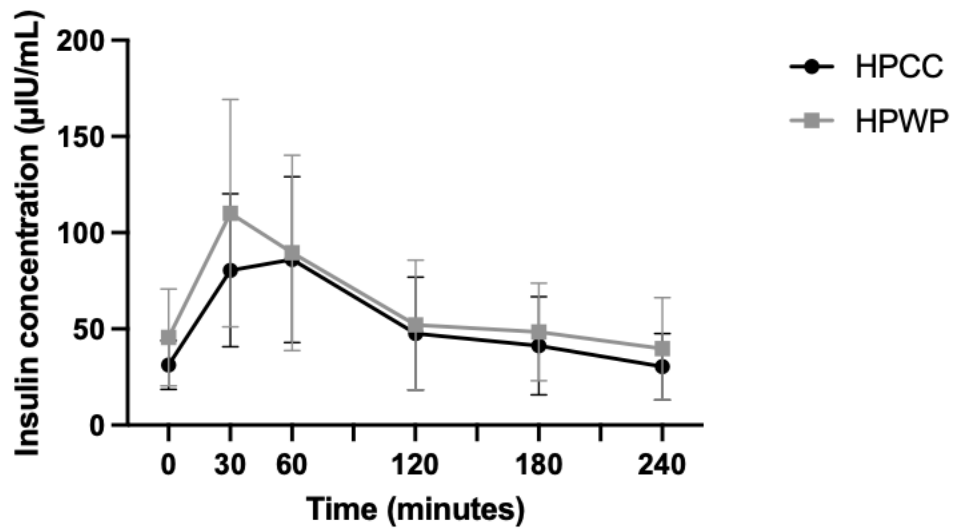


Figure 4. Postprandial insulin response following ingestion of either higher protein test breakfast containing white potatoes or higher protein test breakfast containing a control carbohydrate (white rice). HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=8.

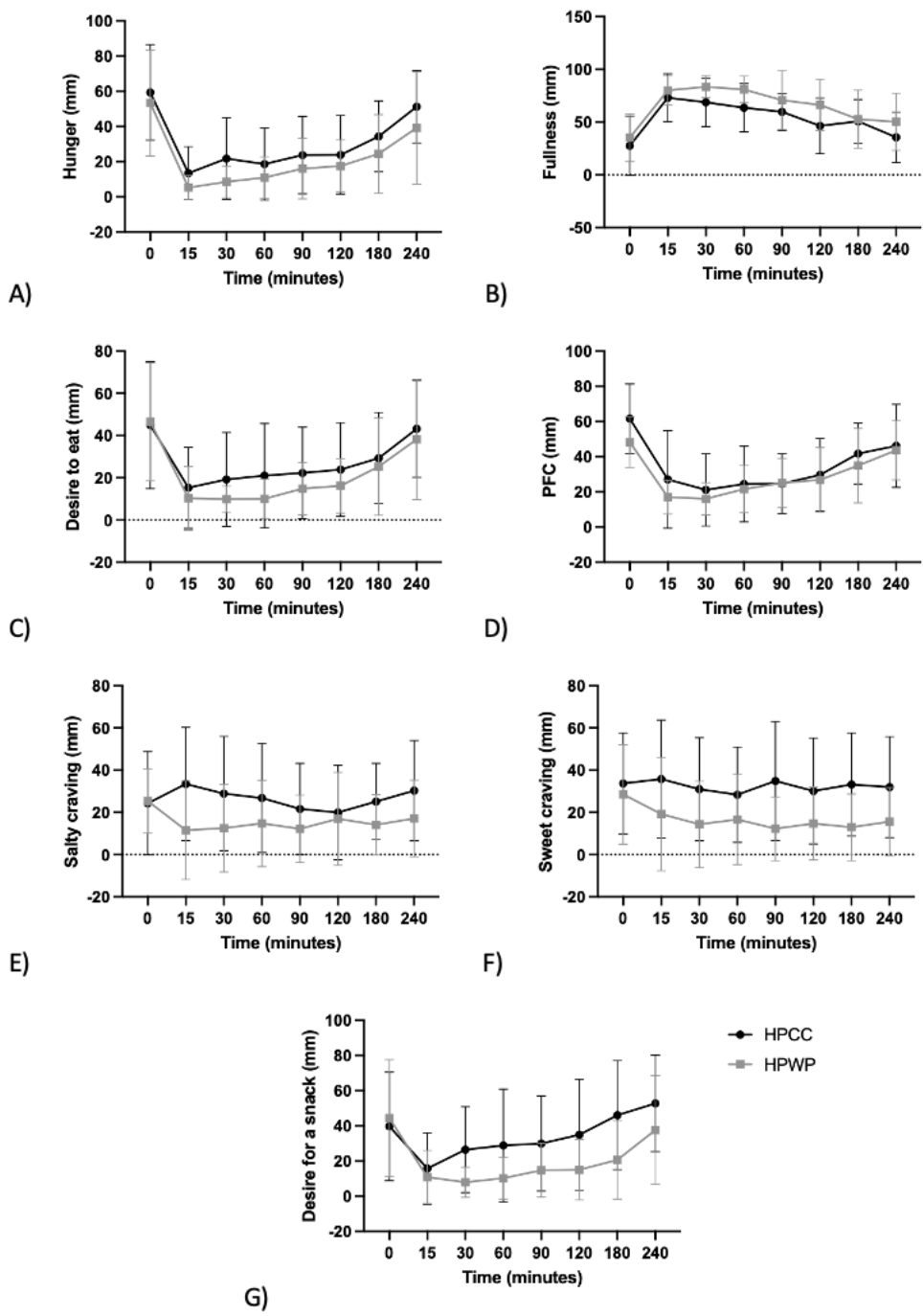


Figure 5. Ratings of perceived appetite assessment following ingestion of either higher protein test breakfast containing white potatoes or higher protein test breakfast containing a control carbohydrate (white rice) using visual analog scales. HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=11. A) “How HUNGRY do you feel at this moment”,

B) How FULL do you feel at this moment”, C) “How STRONG is your desire to eat at this moment”, D) “How MUCH FOOD do you think you could eat at this moment”, E) “How strong is your desire for something SALTY”, F) “How strong is your desire for something SWEET”, G) “How strong is your desire for a SNACK?”

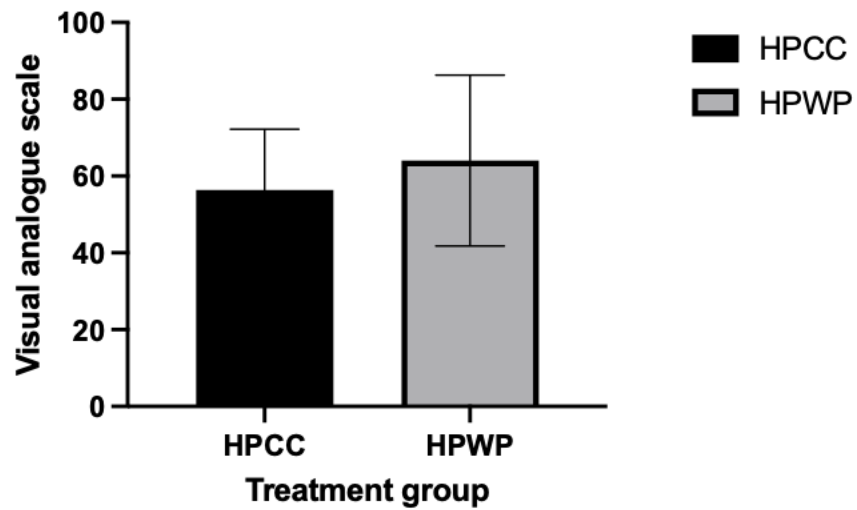


Figure 6. Ratings of perceived palatability following ingestion of either higher protein test breakfast containing white potatoes or higher protein test breakfast containing a control carbohydrate (white rice) using visual analog scales. HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=11. “How much do you like or dislike the taste of the meal?”

Chapter Two Tables

Table 1. Participant demographics¹

| | | HPWP | HPCC |
|---------|------------------|-------------|------------|
| Age (y) | | 40.0 ± 11.7 | 31.5 ± 5.5 |
| Sex | | | |
| | Male | 3 | 4 |
| | Female | 9 | 7 |
| Race | | | |
| | Asian | 1 | 1 |
| | Caucasian | 11 | 6 |
| | African American | 0 | 2 |
| | Hispanic | 0 | 2 |

¹ Values are mean ± SD. HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=11.

Table 2. Participant baseline characteristics¹

| | HPWP | | | HPCC | | |
|--------------------------|--------------|-------------|--------------|-------------|--------------|--------------|
| | Female | Male | Total | Female | Male | Total |
| Anthropometrics | | | | | | |
| Weight (kg) | 102.0 ± 25.2 | 108.0 ± 8.1 | 103.5 ± 22.0 | 97.6 ± 26.0 | 107.2 ± 11.0 | 101.1 ± 21.6 |
| Height (cm) | 159.4 ± 7.2 | 179.8 ± 4.9 | 164.5 ± 11.3 | 161.9 ± 6.0 | 182.6 ± 8.3 | 169.4 ± 12.3 |
| BMI (kg/m ²) | 39.7 ± 8.1 | 33.4 ± 4.1 | 38.2 ± 7.7 | 36.7 ± 7.9 | 32.2 ± 4.1 | 35.1 ± 6.9 |
| WHR | 0.90 ± 0.06 | 1.01 ± 0.05 | 0.93 ± 0.07 | 0.90 ± 0.09 | 1.00 ± 0.03 | 0.94 ± 0.08 |

¹ Values are mean ± SD. HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=11.

Table 3. Nutrient content of test meal

| | HPCC | HPWP |
|------------------------|-------|-------|
| Macronutrient content | | |
| Energy (kcal) | 362 | 367 |
| Carbohydrate (g) | 36 | 36 |
| Fat (g) | 12 | 11 |
| Protein (g) | 27 | 27 |
| Fiber (g) | 0.5 | 4 |
| Amino acid content (g) | | |
| Tryptophan | 0.314 | 0.317 |
| Threonine | 1.110 | 1.125 |
| Isoleucine | 1.527 | 1.515 |
| Leucine | 2.411 | 2.334 |
| Lysine | 1.861 | 1.954 |
| Methionine | 0.873 | 0.858 |
| Cystine | 0.609 | 0.589 |
| Phenylalanine | 1.561 | 1.546 |
| Tyrosine | 1.101 | 1.085 |
| Valine | 1.836 | 1.839 |
| Arginine | 1.612 | 1.539 |
| Histidine | 0.703 | 0.695 |
| Alanine | 1.553 | 1.486 |

| | | |
|---------------|-------|-------|
| Aspartic acid | 2.735 | 3.370 |
| Glutamic acid | 4.159 | 4.159 |
| Glycine | 0.956 | 0.956 |
| Proline | 1.276 | 1.276 |
| Serine | 1.856 | 1.856 |

Table 4. Postprandial plasma glucose and insulin concentrations over time.

| Marker | Time (minutes) | | | | | | | Two-way ANOVA P^2 | | |
|-----------------|----------------|--------------|-------------|-------------|-------------|-------------|--------------------------|---------------------|----------|-------------|
| | 0 | 30 | 60 | 120 | 180 | 240 | Δ | Diet | Time | Time x Diet |
| Glucose (mg/dL) | | | | | | | | 0.96 | <0.0001* | 0.48 |
| HPCC | 84.4 ± 5.6 | 97.8 ± 20.6 | 89.9 ± 17.6 | 74.7 ± 9.2 | 79.6 ± 8.8 | 79.8 ± 8.2 | -4.5 ± 10.6 ^a | | | |
| HPWP | 87.0 ± 5.4 | 99.0 ± 13.3 | 81.1 ± 16.6 | 78.4 ± 11.6 | 78.6 ± 8.4 | 81.0 ± 9.1 | -6.0 ± 12.0 ^a | | | |
| Insulin (μU/mL) | | | | | | | | 0.42 | <0.0001* | 0.40 |
| HPCC | 31.3 ± 12.7 | 80.4 ± 39.7 | 86.0 ± 43.1 | 47.5 ± 29.3 | 41.3 ± 25.5 | 30.3 ± 17.4 | -0.9 ± 12.1 ^a | | | |
| HPWP | 45.6 ± 25.2 | 110.1 ± 59.1 | 89.5 ± 50.7 | 52.0 ± 33.8 | 48.4 ± 25.4 | 39.7 ± 26.5 | -5.9 ± 8.5 ^a | | | |

¹Values are mean ± SD. HPWP, high protein white potato, n=12; HPCC, high protein control carbohydrate, n=8.

²Differences in raw data were analyzed at 0, 30, 60, 120, 180, and 240 minutes using Two-way ANOVA. P-values are indicated for main effects of group and time and an interaction effect of group X time. Significant differences: * P <0.01 and ** P <0.05

Values sharing the same letter are not significantly different.

Chapter 3

Carbohydrate Source as part of a Higher Protein Diet Does Not Affect Body Composition or Cardiometabolic Biomarkers in Adults at Risk for Metabolic Syndrome

Abstract

Background. Obesity-related cardiometabolic dysfunction is a significant public health concern. As of 2018, Metabolic Syndrome (MetS) was estimated to affect as much as twenty five percent of the global population.

Justification. Higher protein diets (HPD) have been shown to improve multiple cardiovascular risk factors. The type of carbohydrate source consumed with higher protein diets and its impact on MetS has not been investigated closely and is therefore a gap in the literature.

Objective and Hypothesis. Determine the long-term effects of carbohydrate source with HPD on markers of MetS. HPD containing white potatoes will improve markers of MetS in individuals at risk for MetS.

Materials and Methods. Participants (n=21; 14 females and 7 males, age = $35.36 \text{ y} \pm 6.17$, BMI = $35.82 \text{ kg/m}^2 \pm 3.29$) were recruited to participate in this 16-week randomized, controlled dietary intervention. To qualify, participants needed two of five criteria of MetS outlined by NCEP ATP III (2005). Upon recruitment, participants were assigned to one of two dietary intervention groups: 1) higher protein intake (30%) and 4-6 meals per week containing white potatoes (HPWP); or 2) higher protein intake (30% of energy) with 4-6 meals per week containing starchy carbohydrates (white rice/pasta) and no potato consumption (HPCC). Participants were instructed to maintain their normal calorie intake and physical activity levels

throughout the study. Participants arrived fasted and anthropometrics and biomarkers of MetS were measured at 0, 4, 8, and 16 weeks. Two-way ANOVA was used to determine the effect of diet, time, and diet over time (p -value ≤ 0.05).

Results. HPWP had significant changes in weight, TC, LDL, lean mass, fat-free mass, and BMC when compared to HPCC. However, no significant differences were seen between dietary treatment groups in measurements of fasting plasma glucose, insulin, or cortisol.

Conclusions. Consumption of a HPD containing white potatoes improved markers of body composition and cholesterol but did not significantly affect cardiometabolic biomarkers of MetS when compared to a HPD containing a control carbohydrate.

Introduction

Obesity has become a significant health problem in the United States and across the globe [1]. Recent findings suggest that approximately 50% of U.S. adults will have obesity and 25% will have severe obesity (body mass index (BMI) $> 40 \text{ kg/m}^2$) by the year 2030 [2]. As rates of obesity increase, so too does prevalence obesity-related diseases, such as the metabolic syndrome. Metabolic syndrome (MetS) is a clustering of cardiometabolic risk factors including insulin resistance (IR), visceral adiposity (VA), atherogenic dyslipidemia (AD), and endothelial dysfunction (ED) [8]. Each risk factor has its own detrimental effects, however, when these risk factors are grouped together they can have an even greater impact [9]. Globally, prevalence of MetS has reached 31%, and is associated with a 1.5-fold increase in the risk of all-cause mortality [31]. If left untreated, the cardiometabolic risk factors of MetS aid in the development of cardiovascular disease (CVD) and type 2 diabetes (T2D) [10].

Currently, there are two primary approaches used to treat and manage MetS: pharmacological and lifestyle (e.g. physical activity, nutrition/dietary intake) modification [11]. Lifestyle modification, especially in the realm of dietary behaviors, is considered the primary therapeutic strategy for treatment and management of MetS [255]. Many different types of dietary interventions and their impact on MetS have been studied in the literature including time restricted feeding and intermittent fasting, as well as the paleolithic, ketogenic, Mediterranean, and high protein diets. Recently, higher protein diets (HPD) have been the subject of much investigation [12-22]. The daily recommended protein intake for adults is 0.80 g/kg body weight/day, (10–15% of macronutrient intake) [35]. However, researchers suggest that the daily recommendation for protein intake should be increased to 20-35% as the benefits of protein intake beyond the recommendations are well-established [33-35].

Studies have shown that habitual consumption of HPD have resulted in reduced body weight and fat mass while preserving more lean mass and increasing energy expenditure when compared to a standard protein diet (SPD). In a 12-week study evaluating performance of a HPD (25% of macronutrient intake) or SPD (15% of macronutrient intake) in 43 overweight and obese men, researchers found that consumption of a HPD aided in the preservation of more muscle mass while experiencing weight loss compared to a standard protein diet [41]. One systematic review and meta-analysis evaluated the effects of high-protein, low fat diets compared to standard-protein, low-fat diets on weight loss, body composition, resting energy expenditure, satiety and appetite, and cardiometabolic biomarkers. Data showed that habitual consumption of an isocalorically prescribed high-protein, low-fat diet showed notable benefits for weight loss, fat loss, and reduction in TRG, while mitigating reductions in fat-free mass [25].

Currently, there has been a significant amount of research done on the topic of HPD and its effect on cardiometabolic biomarkers in a state of weight loss. However, very few studies have been performed to investigate the role of the carbohydrate source in conjunction with a HPD in a state of weight maintenance and its effects on cardiometabolic biomarkers in adults at risk for MetS.

The present study tested the hypothesis that a HPD containing white potatoes will improve body composition and cardiometabolic biomarkers in adults at risk for MetS. To our knowledge, this is the first study to examine the effects of consumption of a HPD with white potatoes or a control carbohydrate (white rice/pasta) on markers of metabolic syndrome in a state of weight maintenance in adults at risk for MetS.

Materials and Methods

Participants and ethical approval. From May 2019 to August 2022, adult male and female participants between the ages of 25 and 50 years old were recruited to participate in this 16-week randomized, controlled, single-blinded dietary intervention (n=26; 17 females and 9 males). There were three phases of the recruitment plan. In the first phase of recruitment, participants were recruited from the Northwest Arkansas area through advertisements posted in the local university daily newsletter (University of Arkansas Newswire), and through advertisements posted within the Northwest Arkansas community, social media, and word-of-mouth. The second phase of recruitment involved a screening questionnaire administered via phone call. Interested participants reached out via email and were scheduled for an initial phone screening. A total of 225 individuals completed the phone screening and 169 individuals

were excluded as they did not meet the enrollment criteria. Individuals who had food allergies or dietary restrictions (vegetarian, Halal/Kosher, low-carbohydrate, gluten free, etc.), were actively trying to lose weight, had lost greater than five percent of their body weight over the past three months, were taking prescription medications, had a body mass index (BMI) less than 25, had any pre-existing cardiometabolic conditions (congestive heart failure, cardiomyopathy, etc.), had chronic mental health issues (depression, anxiety, etc.), or were uncomfortable with/had a fear of needles were excluded from participating in this study. The final phase of recruitment was an in-person clinical screening to assess physical eligibility. Participants who met the initial phone screening criteria underwent an in-person screening at The Center for Human Nutrition (University of Arkansas, Fayetteville, AR) to determine physical eligibility. A total of 56 individuals qualified for the in-person clinical screening. Fourteen individuals failed to confirm their appointment or were absent at their scheduled clinical screening time. The 32 individuals who attended were screened for two or more characteristics of MetS (body mass index (BMI) $> 25 \text{ kg/m}^2$, abdominal obesity (waist-to-hip ratio (WHR) ≥ 0.90 cm in men and ≥ 0.85 cm in women), triglyceride (TRG) level $> 150 \text{ mg/dL}$, HDL cholesterol $< 40 \text{ mg/dL}$ in men and 50 mg/dL in women, systolic blood pressure $\geq 130 \text{ mm Hg}$ or diastolic blood pressure $\geq 85 \text{ mm Hg}$, and/or fasting glucose $> 100 \text{ mg/dL}$). Out of the 32 participants who were clinically screened, a total of 26 participants were recruited and allocated into two treatment groups. Written consent was obtained from all participants prior to beginning the study. Twenty-one men and women were analyzed at the conclusion of the study. Five participants dropped out of the intervention for various reasons including: religious considerations, failed blood collection at baseline, participation in other studies, or lost to

follow up. See **Figure 1** for flow diagram of recruitment and participation. Ethical approval for the study protocol was obtained from the Office of Research Compliance Institutional Review Board of the University of Arkansas (Fayetteville, AR). This trial was registered at clinicaltrials.gov (NCT03935048).

Study design. Participants were assigned to one of two treatments groups: 1) higher protein diet containing white potatoes (HPWP) (n=11, 8 females and 3 males, age 39.7 ± 12.4 y, weight 104.5 ± 22.7 kg, BMI = 38.1 ± 8.1 kg/m²) or 2) higher protein diet with control carbohydrate (HPCC) (n=10, 6 females and 4 males, age = 31.1 ± 5.6 , weight 96.8 ± 17.1 kg, BMI = 33.4 ± 4.6 kg/m²). Refer to **Tables 1 and 2** for participant characteristics and demographics. Each participant completed five study visits at baseline and weeks 4, 8, 12, and 16. At each study visit, participants arrived fasted (10-12 hours) at the Center for Human Nutrition (University of Arkansas) between the hours of 5:30-8:30am for data collection. Upon arrival to each study visit, participants were screened for COVID-19 and their anthropometric and cardiometabolic measurements including body height (cm), body weight (kg), waist measurement (cm), hip measurement (cm), waist-to-hip ratio (WHR), systolic and diastolic blood pressure (mmHg), and pulse rate (bpm) were recorded. Fasting plasma samples were collected by a licensed phlebotomy technician and assessed for cardiometabolic biomarkers. Additionally, participants completed mood and sleep questionnaires that will not be discussed in this manuscript. For objective evaluation of sleep, participants were instructed to wear an ActiGraph activity and sleep monitor on their non-dominant wrist and maintain a sleep diary for seven days at baseline and one week prior to the conclusion of the study. Participants were reminded of their

study day appointments using the RemindApp one day prior to each study visit. Additionally, participants received a weekly newsletter containing healthy recipes and healthful eating advice. Expectations of the study were fully disclosed to the participants prior to consent, and staff members were on hand to address any questions that arose. See **Appendix 2** for study design.

Dietary intervention. In dietary treatment 1, higher protein diet containing white potatoes (HPWP), participants consumed a higher protein diet and consumed 4-6 meals containing white potatoes each week for 16 weeks. In dietary treatment 2, high protein diet without potatoes (HPCC), participants consumed a high protein diet and consumed 4-6 meals containing white rice or pasta each week for 16 weeks. All dietary treatments were isoenergetic within individual participants. Energy content for weight maintenance per individual was calculated using the Harris Benedict equation x 1.35. Each participant was instructed to follow a macronutrient ratio of 30% protein, 30% fat, and 40% carbohydrates. See **Table 3** for example meal plans for both HPWP and HPCC groups.

To ensure compliance, participants received an informational booklet created by the lab personnel containing their study schedule (dates/times), dietary food log examples, reference sheets (i.e. estimating portion size with their hands and how your plate should look (MyPlate)), variety of high protein recipes and meal suggestions, a healthy eating cookbook (American Diabetes Association, VA), measuring cups and spoons (Betty Crocker), food scale (Greater Goods, LLC), measurement conversion refrigerator magnet (Super Club), and diabetic handbook containing a collection of diabetic friendly meal recipes (American Diabetes Association, VA). To

encourage dietary compliance, participants were also given a food item, potatoes (Great Value- medium sized Russet, one pack of 5 lbs) or rice (Minute- ready to cook white rice, one pack of 14 oz) and a \$25 gift card to the local supermarket (Walmart) at baseline and weeks 4, 8, and 12. Participants were instructed to utilize the gift card to assist with dietary compliance.

Body composition measurements. Anthropometrics measurements were recorded at baseline and at 4, 8, 12, and 16 weeks upon arrival at the Center for Human Nutrition. Body height and weight measurements were taken without shoes or extra materials on the subject. Body weight was measured to the nearest 0.05 kg using calibrated balance scales (Detecto, St. Louis, MO). Body height was measured to the nearest 0.1 cm in the free-standing position using a stadiometer (Detecto, St. Louis, MO). Using a standard measuring tape, waist-to-hip ratio was calculated with waist circumference taken at the top of the iliac crest and hip circumference taken around the widest portion of the buttocks.

Body composition. Body composition including fat mass (%), fat-free mass (kg), lean mass (kg), bone mineral density (BMD; g/cm²), and bone mineral content (BMC; kg) was measured via dual energy X-ray absorptiometry (DEXA; Lunar Prodigy, GE Healthcare) at baseline and week 16. All DEXA scans were performed at the Exercise Science Research Center at the University of Arkansas - Fayetteville.

Strength. Strength was assessed at baseline and week 16 via hand-grip strength test using a standard hand-grip dynamometer (Takei Scientific Instruments, Niigata-City, Japan).

Participants were properly fitted to the dynamometer so that the middle finger was at a 90-degree angle, then instructed to squeeze maximally for three seconds. Participants began the hand-grip strength test on the non-dominant hand. A total of three trials were completed on each hand with a 60 second rest period between trials.

Plasma biomarkers. Whole blood samples were collected at each study visit in EDTA vacutainer tubes following an overnight fast of 10-12 hours. The samples were centrifuged at 4°C for 10 minutes at 1800 x g, separated, and stored at -80°C until further analysis. Plasma insulin, glucose, and cortisol concentrations were measured at baseline and weeks, 4, 8, 12, and 16. Cardiometabolic biomarkers were measured via colorimetric (Cayman Chemical Company, Ann Arbor, MI, USA), and Enzyme Immunoassay (Thermo Fischer Scientific, Waltham, MA, USA) using commercially available kits per manufacture instructions.

Dietary intake. To assist with dietary intake assessment, participants were supplied with scales, measuring cups, teaspoons, and descriptive dietary education materials. To assess baseline dietary intake, all subjects were to complete a three-day (two weekdays and one weekend day) weighed food record documenting any food consumed, the amount of food consumed, and the time the food was consumed prior to beginning the study. In addition, participants maintained one three-day food record between each study visit at baseline and weeks 4, 8, and 12 (a total of five, three-day food records). The energy, macronutrient and micronutrient composition of the 3-day food records were analyzed using the Nutrition Data System for Research software

(NDSR; NDS version 2018, Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN).

Statistical analysis. Summary statistics were calculated for all data and data are expressed as mean \pm standard deviation. All data was analyzed using the statistical software GraphPad Prism version 9.0. All statistical tests were two sided with P-values \leq 0.05 used to indicate statistical significance. Differences in height, weight, waist-to-hip ratio (WHR), cardiometabolic biomarkers, and food intake over the 16-week intervention were measured using repeated-measures analysis of variance (ANOVA). Two-way ANOVA was used to determine differences in clinical biomarkers and body composition between diets and the beginning and end of the study.

Results

Participant characteristics. Physical characteristics and demographics of the participants who completed the study are presented in **Tables 1 and 2**, respectively. The HPWP and HPCC groups had a mean age of 39.7 ± 12.2 y and 31.1 ± 5.6 y and were not significantly different. There were also no significant differences in baseline weight (HPWP 104.5 ± 22.7 kg; HPCC 96.8 ± 17.1 kg), height (HPWP 165.2 ± 11.2 cm; HPCC 169.6 ± 12.9 cm), BMI (HPWP 38.1 ± 8.1 kg/m²; HPCC 33.3 ± 4.7 kg/m²), WHR (HPWP 0.92 ± 0.07 ; HPCC 0.95 ± 0.03), fat mass (HPWP $46.8 \pm 7.8\%$; HPCC $43.9 \pm 5.3\%$), fat-free mass (HPWP 55.93 ± 12.44 kg; HPCC 55.15 ± 10.00 kg), and lean mass (HPWP 52.97 ± 12.18 kg; HPCC 51.96 ± 9.42 kg) between groups.

Anthropometrics. Anthropometric measurements including height, weight, BMI, and WHR are represented in **Table 4**. As to be expected, there were no significant effects of time, diet, or time x diet in height for either group over time. There was a significant effect of time x diet on weight ($P = 0.0071$), and BMI ($P = 0.0470$) for HPWP group when compared to the HPCC group over the 16-week dietary intervention. However, there was no significant effect of time, diet, or time x diet in WHR for the HPWP group when compared to the HPCC group. There was also a significant change in weight from baseline between treatment groups (HPWP -1.4 ± 2.0 kg; HPCC 1.3 ± 2.8 kg).

Body composition. Body composition measurements including fat mass, fat-free mass, lean mass, BMD, and BMC are represented in **Table 6**. There was a significant effect of time x diet on lean mass ($P = 0.0216$), fat-free mass ($P = 0.0261$), and BMC ($P = 0.0078$) between the HPWP and HPCC groups over time. There was also a significant change in lean mass (HPWP -0.61 ± 2.11 kg; HPCC 1.51 ± 1.72 kg), fat-free mass (HPWP -0.54 ± 2.01 kg; HPCC 1.44 ± 1.71 kg), and BMC (HPWP 0.06 ± 0.12 kg; HPCC -0.28 ± 0.36 kg) between treatment groups. There was no significant effect of time, diet, or time x diet on fat mass or BMD between treatment groups.

Strength. Hand-grip strength measurements for both the dominant and non-dominant hands are represented in **Table 6**. There was a significant effect of time on hand-grip strength in the dominant hand ($P = 0.0156$) in both the HPWP and HPCC groups. However, there was no significant effect of time, diet, or time x diet in hand-grip strength of the non-dominant hand in either group.

Cardiometabolic biomarkers. Cardiometabolic measurements including TC (HDL and LDL), TRG, SYS, and DIA blood pressure are represented in **Table 5**. There was a significant effect of time x diet on TC ($P < 0.0037$), however there were no significant effects of time, diet, or time x diet for HDL, LDL, TRG, or SYS and DIA blood pressure between groups over time. There was a significant change in TC (HPWP -15.4 ± 12.3 mg/dL; HPCC 6.7 ± 12.7 mg/dL) and LDL (HPWP -18.9 ± 18.7 mg/dL; HPCC 3.1 ± 9.4 mg/dL) between groups over time. Fasting plasma glucose, insulin, and cortisol results are presented in **Table 7**. Additionally, fasting plasma glucose, insulin, and cortisol results are graphically presented in **Figures 2, 3, and 4** respectively. There was a significant difference ($P < 0.01$) in fasting plasma cortisol concentrations between the HPWP and HPCC groups. However, there was no significant effect of time, diet, or time x diet on any of fasting plasma glucose, insulin, or cortisol concentrations in either of the treatment groups.

Dietary intake.

Average dietary intakes for both the HPWP and HPCC groups are represented in **Table 8**. There was a significant effect of time ($P < 0.01$) on average intake of energy (kcal), carbohydrates, and protein ($P < 0.05$). There was a significant difference ($P < 0.01$) in average intake of protein between the HPWP and HPCC groups. There was only a significant effect of time x diet ($P < 0.01$) on average intake of fat when comparing groups.

Discussion

To our knowledge, this is the first study to examine the effects of carbohydrate source (white potatoes and white rice/pasta) on markers of metabolic syndrome in a state of weight maintenance in adults at risk for MetS. The present study tested the hypothesis that a HPD containing white potatoes will improve body composition and cardiometabolic biomarkers in adults at risk for MetS. Our results indicate that a HPD containing white potatoes leads to significant changes in body composition and cholesterol, but not cardiometabolic biomarkers when compared to a HPD containing a control carbohydrate (white rice/pasta). Collectively, this data suggests that in adults at risk of MetS, carbohydrate source will affect body composition and cardiometabolic biomarkers of MetS.

It is acknowledged in the literature that long-term consumption of a HPD is associated weight loss, improved glucose homeostasis, and increased energy expenditure and fat oxidation [286, 287]. There has been a considerable amount of research done on the topic of HPD and its effect on cardiometabolic biomarkers in a state of weight loss. However, very few studies have been performed to investigate the role of the carbohydrate source in conjunction with a HPD in a state of weight maintenance and its effects on cardiometabolic biomarkers in adults at risk for MetS.

White potatoes are often denigrated in nutrition circles due to their frequent association with high fat diets. Typically, consumers believe that white potatoes are higher in fat and calories than other carbohydrates sources such as rice or pasta. However, white potatoes have a similar nutrient composition to that of white rice, though white potatoes have greater amount of certain vitamins and minerals [317]. The white potato is indeed an excellent

source of key nutrients such as carbohydrate, dietary fiber, vitamin B6, vitamin C, and potassium [317, 318].

Participants who consumed a HPD containing white potatoes experienced loss of body weight when compared to participants who consumed a HPD containing a control carbohydrate (white rice/pasta), who gained body weight. In addition, the HPWP group also decreased in BMI compared to the HPCC group, although this change was not significant. This is interesting, as all dietary treatments were calculated to be euenergetic for weight maintenance (Harris Benedict equation $\times 1.35$) within individual participants. Although, the HPWP group consumed comparable amounts of energy to the HPCC group, the HPWP group consumed greater amounts of protein than the HPCC group. These results align with a 6-month randomized dietary intervention involving fifty participants who were prescribed a HPD (25% of macronutrient intake), high-carbohydrate diet (protein as 12% of total macronutrient intake), or control group (fat intake as 30% of total macronutrient intake). At the conclusion of the intervention, participants in the HPD group had more significant reductions in body weight (-7.3 ± 11.9 kg) compared to other treatments groups (-3.6 ± 6.4 kg) [293]. In a separate study involving 105 participants consuming a HPD (1.34 g/kg body weight) or a SPD (0.8 g/kg body weight), participants consuming a HPD experienced significantly greater body weight loss (-7.0 ± 3.7 kg) after six months than participants consuming a SPD (-5.1 ± 3.6 kg) [297]. However, participants in the aforementioned study were prescribed a caloric deficit of 500 kcals for weight loss, whereas the current study prescribed a caloric intake calculated for weight maintenance via the Harris Benedict equation [329]. In addition, previous research has suggested that consumption of white potatoes in a mixed meal will reduce glycemic index and

increase postprandial satiety [319-322, 330]. Therefore, the HPWP group may have experienced greater loss of weight and BMI due to the effects of dietary protein on satiety in addition to the effects of white potato consumption.

In addition, participants in the HPWP group experienced a significant reduction in TC and LDL over the course of the 16-week intervention. The participants in the HPCC group, however, experienced an increase in TC and LDL throughout the intervention. These results align with results of a previous study performed in mice that suggest consumption of white potatoes in a mixed meal will lead to lowering of TC [331].

Participants in the HPWP group showed a decrease in fat-free mass and lean mass compared to the HPCC group. These results make sense, as a decrease in fat-free mass and lean mass is associated with weight loss [332]; and the HPWP group decreased in body weight over the 16-week intervention. The HPWP group increased in BMC compared to participants in the HPCC group. The HPWP group also increased BMD, though the difference was not significant. It is possible that consumption of white potatoes resulted in the increase in BMC in the HPWP group, as it is acknowledged that white potatoes are an excellent source of minerals, and will result in increased BMD and BMC [333].

Hand-grip strength improved in the dominant hand for both the HPWP and HPCC groups over the 16-week intervention, although the difference was not significant. This can likely be attributed to the higher protein intervention, as participants experienced increases in hand-grip strength throughout the study, independently of carbohydrate source. Interestingly, hand-grip strength for the non-dominant hand did not show any significant effects over the 16-week intervention for either group, despite improved strength over time in the dominant hand.

No significant differences were found in fasting measurements of plasma glucose and insulin between the HPWP and HPCC groups. Fasting plasma insulin results align with results of a study involving nineteen adults at risk for T2D. Results of the aforementioned study showed that insulin sensitivity was not significantly different between the white potato group and control group [334]. Fasting plasma glucose results of the current study contradict previous research performed in mice, which suggests that consumption of white potatoes will contribute to glucose lowering [319, 335]. In addition, participants in the HPWP also had significantly higher plasma cortisol concentrations than the HPCC group, however, this was not a result of the dietary intervention as the cortisol concentrations were significantly different at baseline and throughout the entire intervention.

To our knowledge, this is one of the first long-term studies to examine the role of the carbohydrate source with a HPD on cardiometabolic biomarkers of metabolic syndrome in adults at risk for MetS. However, there are several limitations to this study. Although recruitment aimed to balance gender between treatment groups, both treatment groups primarily consisted of females (HPWP; 8 females and 3 males, HPCC; 6 females and 4 males). The sample size of this study was small (n=21). Ninety percent of individuals who were screened to participate in this study did not meet the criteria for inclusion. Therefore, this study should be considered a pilot study. Both groups were at least 50% Caucasian (HPWP; 11, HPCC; 5), however the HPCC group was more diverse than the HPWP group. The HPWP group had at least one participant in each of Asian, African American, Caucasian, and Hispanic categories, whereas the HPCC group was less diverse, with only one non-Caucasian participant (Asian). Perhaps the most influential of the limitations of the current study is the incongruence between

the prescribed macronutrient ratio and the macronutrient ratio that the participants actually consumed. Each participant was instructed to follow a macronutrient ratio of 30% protein, 30% fat, and 40% carbohydrates, however, the HPWP group consumed 19.1% protein, 38.9% carbohydrates, and 42.6% fat, while the HPCC consumed 17.7% protein, 45.6% carbohydrates, and 36.6% fat. Indeed, it is common to encounter underreporting of dietary intake in many nutritional studies, especially in those relating diet to obesity or obesity-related disorders [336]. However, the question still arises whether the results of the current study can truly be related to HPDs. It is true that the actual protein consumption for both the HPWP and HPCC groups was lower than prescribed, however, according to the Centers for Disease Control and Prevention, the average protein intake among adults aged 20 and over was 15.8% as of 2018 [337]. Therefore, participants in the current study were still consistently consuming greater-than-average amounts of protein, and results may still be applicable to higher protein intake. Regardless, this could have been a contributing factor in the lack of improvement in other cardiometabolic biomarkers between the dietary treatment groups. Future research should focus on whether consumption of a strict HPD containing white potatoes shows improvement in cardiometabolic biomarkers of MetS compared to a HPD containing a control carbohydrate (white rice/pasta).

Conclusion

Collectively, no definitive conclusions can be made on the basis of a HPD, as the participants in the current study were not following a strict HPD. In the current study, participants in the HPWP group experienced significant changes in body composition and

cholesterol, but not other cardiometabolic biomarkers when compared to participants in the HPCC group. There is potential for carbohydrate source to be useful in treatment of markers of MetS. Future research should focus on strict monitoring of dietary intake of the participants, and equal number of men and women in each group. Additional research is necessary to understand the role of carbohydrate intake with a HPD in adults at risk for MetS.

Chapter Three Figures

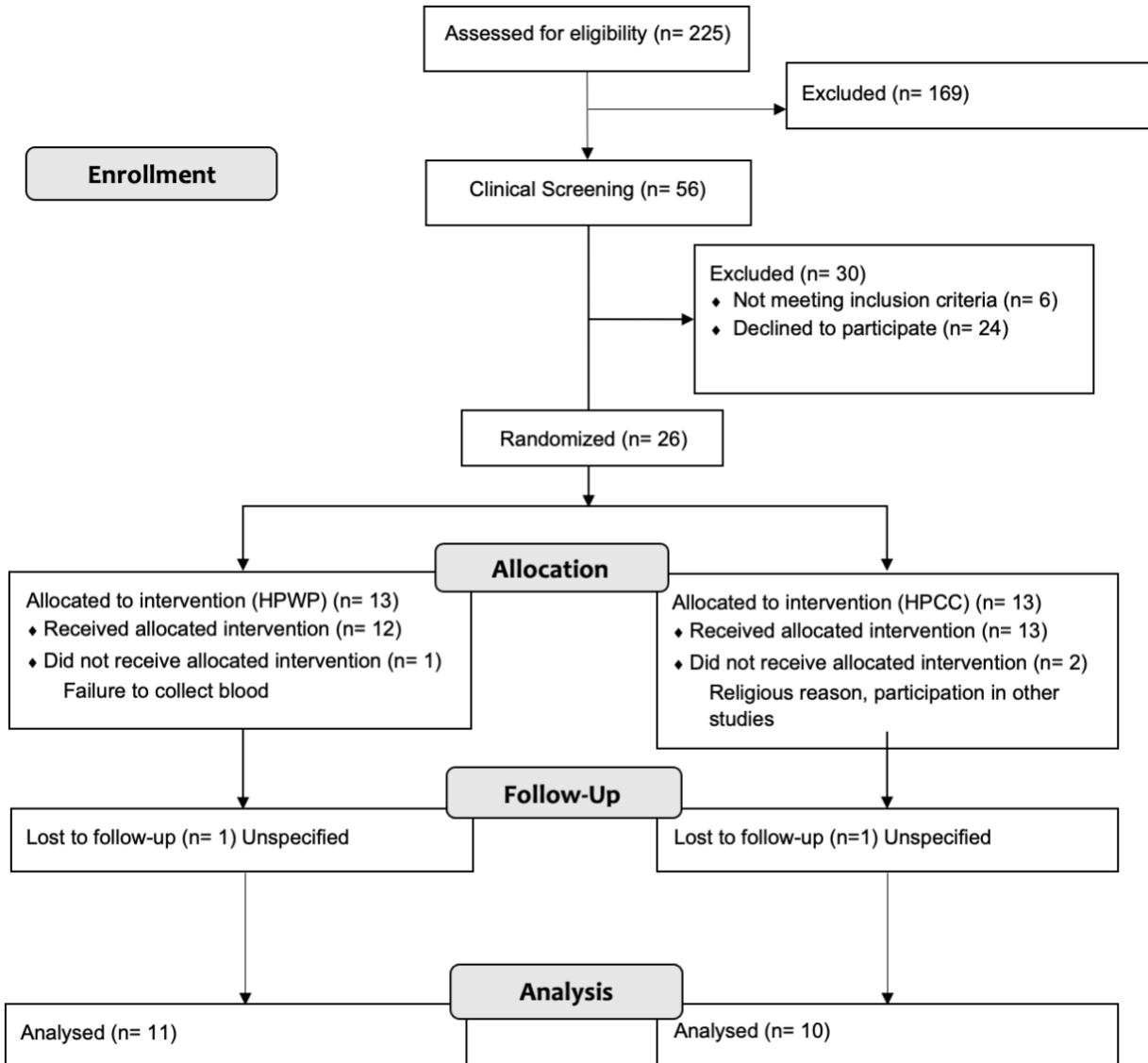


Figure 1. Flow chart showing number of subjects recruited and their attrition patterns during the dietary intervention study. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10. Reason for subject withdrawal were as follows: failure to collect blood at baseline (1), participation in Ramadan fasting (1), unexpected participation in other studies (1), and unspecified (2).

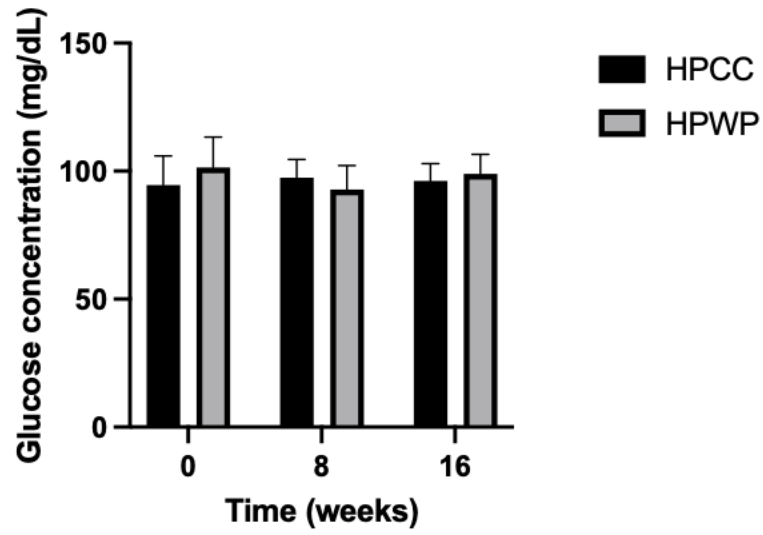


Figure 2. Fasting plasma glucose concentrations as a result of 16-week dietary intervention. HPWP, high protein white potato, n=10; HPCC, high protein control carbohydrate, n=8.

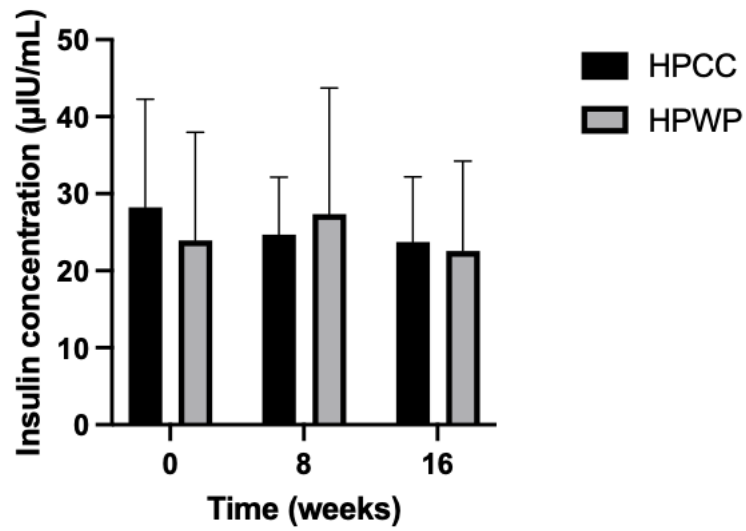


Figure 3. Fasting plasma insulin concentrations as a result of 16-week dietary intervention. HPWP, high protein white potato, n=10; HPCC, high protein control carbohydrate, n=8.

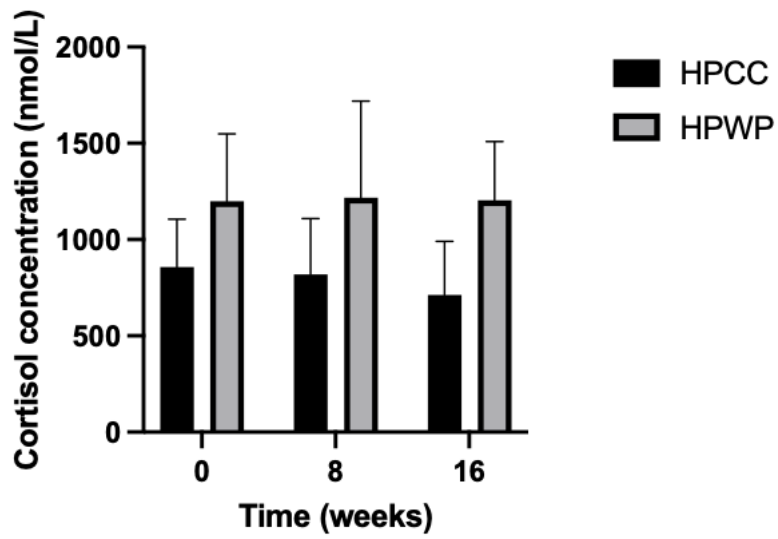


Figure 4. Fasting plasma cortisol concentrations as a result of 16-week dietary intervention. HPWP, high protein white potato, n=10; HPCC, high protein control carbohydrate, n=8.

Chapter Three Tables

Table 1. Participant baseline characteristics¹

| | HPWP | | | HPCC | | |
|--------------------------|--------------|-------------|---------------|-------------|--------------|--------------|
| | Female | Male | Total | Female | Male | Total |
| Anthropometrics | | | | | | |
| Weight (kg) | 103.5 ± 26.7 | 108.0 ± 8.1 | 104.5 ± 22.7 | 89.8 ± 17.5 | 107.2 ± 11.0 | 96.8 ± 17.1 |
| Height (cm) | 164.2 ± 7.3 | 179.8 ± 4.9 | 165.2 ± 11.2 | 160.8 ± 5.9 | 182.6 ± 8.3 | 169.6 ± 12.9 |
| BMI (kg/m ²) | 38.3 ± 8.6 | 33.4 ± 4.1 | 38.1 ± 8.1 | 34.4 ± 5.3 | 32.2 ± 4.1 | 33.3 ± 4.7 |
| WHR | 0.91 ± 0.05 | 1.01 ± 0.05 | 0.92 ± 0.07 | 0.94 ± 0.03 | 1.00 ± 0.03 | 0.95 ± 0.03 |
| Body composition | | | | | | |
| Fat mass (%) | 50.5 ± 4.1 | 36.7 ± 6.0 | 46.8 ± 7.8 | 46.4 ± 4.7 | 40.1 ± 5.3 | 43.9 ± 5.3 |
| Fat-free mass (kg) | 51.2 ± 11.1 | 68.5 ± 3.7 | 55.39 ± 12.4 | 48.9 ± 9.7 | 64.5 ± 3.8 | 55.15 ± 10.0 |
| Lean mass (kg) | 48.4 ± 10.9 | 65.3 ± 3.6 | 52.97 ± 12.18 | 46.1 ± 9.4 | 60.7 ± 3.5 | 51.96 ± 9.42 |

¹Values are mean ± SD. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10.

Table 2. Participant demographics¹

| | HPWP | HPCC |
|------------------|-------------|------------|
| Age (y) | 39.7 ± 12.2 | 31.0 ± 5.6 |
| Sex | | |
| Male | 3 | 4 |
| Female | 8 | 6 |
| Race | | |
| Asian | 1 | 1 |
| Caucasian | 10 | 5 |
| African American | 0 | 2 |
| Hispanic | 0 | 2 |

¹Values are mean ± SD. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10.

Table 3. Example meal plan

| | HPWP | HPCC |
|-----------------------|---|--|
| Breakfast | 1 cup coffee (black) 2 Tbsp sugar 2 large eggs 4 slices turkey bacon 2 slices sourdough bread | 1 cup egg whites 0.5 cup mini peppers 0.5 cup onion 0.5 cup black beans 1 cup spinach 1 slice sourdough bread |
| Snack 1 | 1 oz. roasted almonds | 1 cup vanilla nonfat Greek yogurt |
| Lunch | 1 whole grain and flax tortilla wrap 2 slices baby Swiss cheese 10 slices deli meat (turkey) | 1 chickpea burger 1 cup lettuce 1 slice baby Swiss cheese 1 hamburger bun 1 cup sweet potato fries |
| Snack 2 | 1 cup vanilla nonfat Greek yogurt 1.5 cups strawberries | 1 oz. turkey jerky |
| Dinner | 2 chicken breasts 1 baked russet potato 2 cups cooked broccoli 0.5 Tbsp salted butter | 1 cup white rice 6 oz. skirt steak 0.5 cup chopped carrots 100 grams bean sprouts 1 Tbsp soy sauce |
| Total calories (kcal) | 1839 kcal | 1836 kcal |
| | 149 g P, 163 g C, 63 g F | 145 g P, 186 g C, 63 g F |

Table 4. Physical characteristics of adults at risk for MetS over 16-week dietary intervention¹

| Marker | Time (weeks) | | | | | | Two-way ANOVA <i>P</i> ² | | |
|--------------------------|--------------|--------------|--------------|--------------|--------------|---------------------------|-------------------------------------|------|-------------|
| | 0 | 4 | 8 | 12 | 16 | Δ | Diet | Time | Time x Diet |
| Height (cm) | | | | | | | 0.42 | 0.44 | 0.34 |
| HPCC | 169.6 ± 13.0 | 169.5 ± 13.0 | 169.5 ± 13.1 | 169.8 ± 12.8 | 169.8 ± 12.8 | 0.3 ± 1.0 ^a | | | |
| HPWP | 165.4 ± 11.4 | 165.3 ± 11.3 | 165.5 ± 11.9 | 165.3 ± 11.3 | 165.3 ± 11.3 | -0.1 ± 0.2 ^a | | | |
| Weight (kg) | | | | | | | 0.49 | 0.26 | <0.01* |
| HPCC | 96.8 ± 17.1 | 96.8 ± 16.4 | 97.2 ± 17.2 | 97.2 ± 17.4 | 98.1 ± 17.7 | 1.3 ± 2.8 ^a | | | |
| HPWP | 104.5 ± 22.7 | 103.5 ± 23.1 | 102.9 ± 24.3 | 103.0 ± 22.5 | 103.2 ± 23.0 | -1.4 ± 2.0 ^b | | | |
| BMI (kg/m ²) | | | | | | | 0.17 | 0.18 | 0.04** |
| HPCC | 33.5 ± 4.7 | 33.5 ± 4.6 | 33.8 ± 4.8 | 33.6 ± 4.8 | 33.9 ± 4.7 | 0.4 ± 1.1 ^a | | | |
| HPWP | 38.1 ± 8.0 | 37.8 ± 8.1 | 37.5 ± 8.6 | 37.6 ± 7.8 | 37.7 ± 8.1 | -0.4 ± 0.8 ^a | | | |
| WHR | | | | | | | 0.16 | 0.11 | 0.34 |
| HPCC | 0.96 ± 0.04 | 0.95 ± 0.04 | 0.95 ± 0.5 | 0.96 ± 0.05 | 0.94 ± 0.04 | -0.03 ± 0.03 ^a | | | |
| HPWP | 0.92 ± 0.07 | 0.92 ± 0.07 | 0.91 ± 0.06 | 0.92 ± 0.06 | 0.92 ± 0.06 | -0.01 ± 0.03 ^a | | | |

¹Values are mean ± SD. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10.

²Differences in raw data were analyzed at 0, 8, and 16 using Two-way ANOVA. P-values are indicated for main effects of group and time and an interaction effect of group X time. Significant differences: **P*<0.01 and ***P*<0.05

Values sharing the same letter are not significantly different.

Table 5. Cardiometabolic biomarkers in adults at risk for MetS¹

| Marker | Time (weeks) | | | | | | Two-way ANOVA <i>P</i> ² | | |
|--------------|--------------|--------------|--------------|--------------|--------------|---------------------------|-------------------------------------|------|-------------|
| | 0 | 4 | 8 | 12 | 16 | Δ | Diet | Time | Time x Diet |
| TC (mg/dL) | | | | | | | 0.62 | 0.41 | <0.01* |
| HPCC | 185.3 ± 49.6 | 174.0 ± 52.8 | 185.7 ± 41.2 | 189.7 ± 50.0 | 192.0 ± 50.5 | 6.7 ± 12.7 ^a | | | |
| HPWP | 202.8 ± 41.9 | 185.0 ± 18.7 | 198.0 ± 41.1 | 190.1 ± 42.9 | 187.5 ± 35.8 | -15.4 ± 12.3 ^b | | | |
| HDL (mg/dL) | | | | | | | 0.43 | 0.67 | 0.33 |
| HPCC | 33.3 ± 14.4 | 35.0 ± 10.8 | 38.7 ± 15.4 | 35.1 ± 12.0 | 37.4 ± 12.3 | 4.1 ± 5.9 ^a | | | |
| HPWP | 36.0 ± 9.0 | 30.8 ± 9.3 | 31.6 ± 9.8 | 31.4 ± 9.4 | 33.0 ± 10.3 | -3.0 ± 13.2 ^a | | | |
| LDL (mg/dL) | | | | | | | 0.11 | 0.33 | 0.12 |
| HPCC | 109.3 ± 26.5 | 105.7 ± 21.7 | 110.9 ± 22.4 | 113.9 ± 19.7 | 112.4 ± 25.9 | 3.1 ± 9.4 ^a | | | |
| HPWP | 143.6 ± 41.8 | 124.8 ± 24.9 | 137.8 ± 31.9 | 134.9 ± 41.9 | 124.7 ± 30.5 | -18.9 ± 18.7 ^b | | | |
| TRG (mmol/L) | | | | | | | 0.46 | 0.46 | 0.07 |
| HPCC | 132.8 ± 81.6 | 120.6 ± 73.0 | 119.4 ± 58.1 | 127.3 ± 77.9 | 133.3 ± 75.8 | 0.6 ± 39.8 ^a | | | |
| HPWP | 131.4 ± 37.1 | 151.6 ± 38.9 | 150.7 ± 42.0 | 133.7 ± 50.8 | 149.5 ± 41.7 | 18.1 ± 30.2 ^a | | | |
| SYS (mmHg) | | | | | | | 0.38 | 0.08 | 0.24 |
| HPCC | 126.7 ± 10.3 | 123.1 ± 8.1 | 125.1 ± 7.8 | 125.2 ± 7.4 | 126.2 ± 8.0 | -0.5 ± 7.2 ^a | | | |
| HPWP | 128.8 ± 16.9 | 120.0 ± 13.9 | 118.6 ± 11.8 | 120.6 ± 11.8 | 119.2 ± 10.9 | -9.5 ± 17.4 ^a | | | |
| DIA (mmHg) | | | | | | | 0.87 | 0.13 | 0.50 |
| HPCC | 79.6 ± 9.6 | 79.3 ± 8.1 | 76.6 ± 9.2 | 79.5 ± 10.8 | 77.7 ± 9.2 | -1.9 ± 7.0 ^a | | | |
| HPWP | 81.6 ± 10.7 | 75.8 ± 7.8 | 77.3 ± 8.1 | 78.2 ± 7.5 | 77.8 ± 9.0 | -3.8 ± 9.1 ^a | | | |

¹Values are mean ± SD. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10.

²Differences in raw data were analyzed at 0, 8, and 16 using Two-way ANOVA. P-values are indicated for main effects of group and time and an interaction effect of group X time. Significant differences: **P*<0.01 and ***P*<0.05

Values sharing the same letter are not significantly different.

Table 6. Body composition markers of adults at risk for MetS as a result of dietary intervention¹

| Marker | Time (weeks) | | | Two-way ANOVA <i>P</i> ² | | |
|--------------------------|---------------|---------------|----------------------------|-------------------------------------|--------|-------------|
| | 0 | 16 | Δ | Diet | Time | Time x Diet |
| Lean mass (kg) | | | | 0.99 | 0.30 | 0.02** |
| HPCC | 51.96 ± 9.42 | 53.47 ± 10.18 | 1.51 ± 1.72 ^a | | | |
| HPWP | 52.97 ± 12.18 | 52.35 ± 12.41 | -0.61 ± 2.11 ^b | | | |
| Fat mass (%) | | | | 0.27 | 0.17 | 0.19 |
| HPCC | 43.9 ± 5.3 | 42.8 ± 5.2 | -1.08 ± 1.9 ^a | | | |
| Fat-free mass (kg) | | | | 0.97 | 0.29 | 0.03** |
| HPCC | 55.15 ± 10.00 | 56.58 ± 10.80 | 1.44 ± 1.71 ^a | | | |
| HPWP | 55.93 ± 12.44 | 55.39 ± 12.68 | -0.54 ± 2.01 ^b | | | |
| BMD (g/cm ²) | | | | 0.91 | 0.94 | 0.51 |
| HPCC | 1.30 ± 0.11 | 1.30 ± 0.09 | -0.008 ± 0.49 ^a | | | |
| HPWP | 1.30 ± 0.12 | 1.31 ± 0.10 | 0.006 ± 0.05 ^a | | | |
| BMC (kg) | | | | 0.67 | 0.07 | <0.01* |
| HPCC | 3.25 ± 0.69 | 2.96 ± 0.74 | -0.28 ± 0.36 ^a | | | |
| HPWP | 2.97 ± 0.47 | 3.03 ± 0.42 | 0.06 ± 0.12 ^b | | | |
| Handgrip (D) (kg) | | | | 0.38 | 0.02** | 0.07 |
| HPCC | 35.4 ± 11.6 | 39.2 ± 13.8 | 3.8 ± 4.2 ^a | | | |
| HPWP | 32.9 ± 8.9 | 33.5 ± 8.0 | 0.6 ± 3.3 ^a | | | |

| Handgrip (ND) (kg) | | | | 0.52 | 0.38 | 0.14 |
|--------------------|-------------|-------------|-------------------------|------|------|------|
| HPCC | 34.4 ± 12.1 | 36.5 ± 13.4 | 2.2 ± 4.4 ^a | | | |
| HPWP | 32.5 ± 10.8 | 31.9 ± 9.2 | -0.6 ± 3.8 ^a | | | |

¹Values are mean ± SD. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10.

²Differences in raw data were analyzed at 0 and 16 using Two-way ANOVA. P-values are indicated for main effects of group and time and an interaction effect of group X time. Significant differences: **P*<0.01 and ***P*<0.05

Values sharing the same letter are not significantly different.

Table 7. Cardiometabolic plasma biomarkers measurements of adults at risk for MetS¹

| Marker | Time (weeks) | | | | Two-way ANOVA <i>P</i> ² | | |
|-------------------|----------------|----------------|----------------|-----------------------------|-------------------------------------|------|-------------|
| | 0 | 8 | 16 | Δ | Diet | Time | Time x Diet |
| Glucose (mg/dL) | | | | | 0.55 | 0.49 | 0.09 |
| HPCC | 94.6 ± 11.3 | 97.4 ± 7.1 | 96.2 ± 6.8 | 1.6 ± 9.1 ^a | | | |
| HPWP | 101.5 ± 11.9 | 92.8 ± 9.4 | 98.9 ± 7.7 | -2.5 ± 13.1 ^a | | | |
| Insulin (μIU/mL) | | | | | 0.83 | 0.44 | 0.48 |
| HPCC | 28.2 ± 14.0 | 24.7 ± 7.4 | 23.7 ± 8.5 | -4.5 ± 16.0 ^a | | | |
| HPWP | 23.9 ± 14.0 | 27.4 ± 16.4 | 22.6 ± 11.7 | -1.4 ± 8.8 ^a | | | |
| Cortisol (nmol/L) | | | | | <0.01* | 0.77 | 0.78 |
| HPCC | 857.1 ± 248.0 | 819.1 ± 289.3 | 711.9 ± 279.4 | -145.2 ± 281.9 ^a | | | |
| HPWP | 1199.6 ± 349.2 | 1217.0 ± 501.8 | 1204.5 ± 304.9 | 5.0 ± 465.2 ^a | | | |

¹Values are mean ± SD. HPWP, high protein white potato, n=10; HPCC, high protein control carbohydrate, n=8.

²Differences in raw data were analyzed at 0, 8, and 16 using Two-way ANOVA. P-values are indicated for main effects of group and time and an interaction effect of group X time. Significant differences: **P*<0.01 and ***P*<0.05

Values sharing the same letter are not significantly different.

Table 8. Average dietary intake during dietary intervention of adults at risk for MetS¹

| | Time (weeks) | | | | Two-way ANOVA <i>P</i> ² | | |
|-----------------------|----------------|----------------|----------------|----------------|-------------------------------------|--------|-------------|
| | 0 | 8 | 16 | Δ | Diet | Time | Time x Diet |
| Macronutrient content | | | | | | | |
| Energy (kcal) | | | | | 0.80 | <0.01* | 0.84 |
| HPCC | 2108.7 ± 696.1 | 1735.8 ± 535.5 | 1689.3 ± 393.2 | -419.4 ± 296.6 | | | |
| HPWP | 2076.4 ± 852.6 | 1682.4 ± 527.4 | 1752.3 ± 473.8 | -324.2 ± 229.2 | | | |
| Carbohydrate (g) | | | | | 0.05 | <0.01* | 0.93 |
| HPCC | 240.0 ± 92.5 | 195.4 ± 92.0 | 195.0 ± 57.3 | -45.1 ± 31.9 | | | |
| HPWP | 226.5 ± 109.3 | 154.9 ± 39.3 | 154.3 ± 47.8 | -72.2 ± 51.1 | | | |
| Fat (g) | | | | | 0.34 | 0.35 | 0.01** |
| HPCC | 88.6 ± 27.6 | 69.6 ± 22.9 | 67.1 ± 16.5 | -21.4 ± 15.2 | | | |
| HPWP | 94.4 ± 46.1 | 78.1 ± 29.9 | 88.4 ± 27.2 | -6.0 ± 4.2 | | | |
| Protein (g) | | | | | <0.01* | 0.04** | 0.12 |
| HPCC | 83.7 ± 34.9 | 82.1 ± 24.3 | 78.6 ± 18.3 | -5.1 ± 3.6 | | | |
| HPWP | 82.3 ± 26.1 | 92.1 ± 33.0 | 89.1 ± 29.4 | 6.8 ± 4.8 | | | |
| Fiber (g) | | | | | 0.19 | 0.30 | 0.63 |
| HPCC | 17.1 ± 7.2 | 16.0 ± 4.8 | 16.2 ± 6.8 | -0.90 ± 0.6 | | | |
| HPWP | 28.0 ± 29.8 | 22.5 ± 12.7 | 17.9 ± 8.2 | -10.1 ± 7.2 | | | |

¹Values are mean ± SD. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10.

²Differences in raw data were analyzed at 0, 8, and 16 using Two-way ANOVA. P-values are indicated for main effects of group and time and an interaction effect of group X time. Significant differences: * $P < 0.01$ and ** $P < 0.05$

Conclusion

Obesity has become a major health crisis in the United States and across the globe [1]. Recent findings suggest that approximately 50% of U.S. adults will have obesity and 25% will have severe obesity (body mass index (BMI) > 40 kg/m²) by the year 2030 [2]. As rates of obesity increase, so too does prevalence of obesity-related cardiometabolic [3, 4]. As of 2018, MetS was estimated to affect as much as 25% of the global population [7]. Metabolic syndrome (MetS) is a grouping of cardiometabolic risk factors including insulin resistance (IR), visceral adiposity (VA), atherogenic dyslipidemia (AD), and endothelial dysfunction (ED) [8]. Each risk factor has its own detrimental effects, however, when these risk factors are clustered together they can have an even greater impact [9]. If left untreated, the cardiometabolic risk factors of MetS aid in the pathogenesis of cardiovascular disease (CVD) and type 2 diabetes (T2D) [10]. Much research has been done to evaluate HPD as a potential treatment method to improve markers of MetS. Studies performed to evaluate short-term consumption of HPD show that HPD result in appetite suppression through decreased levels of orexigenic hormones and increased level of anorexigenic hormones, elevated plasma amino acid levels, increased hepatic gluconeogenesis, and increased ketogenesis from the higher protein intake and increased energy expenditure through increased diet-induced thermogenesis [23, 24]. Studies performed to evaluate long-term consumption of a HPD show that HPD result in reduced body weight and fat mass while preserving more lean mass and increasing energy expenditure when compared to a standard protein diet (SPD) [25-30].

Currently, there has been a significant amount of research done on the topic of HPD and its effect on cardiometabolic biomarkers in a state of weight loss. However, very few studies

have been performed to investigate the role of the carbohydrate source in conjunction with a HPD in a state of weight maintenance and its effects on cardiometabolic biomarkers in adults at risk for MetS. Therefore, the objective of this thesis was to determine the role of the carbohydrate source with a HPD on cardiometabolic biomarkers in adults at risk for MetS. The central hypothesis tested in this thesis was that consumption of a HPD containing white potatoes would improve cardiometabolic biomarkers of MetS in adults at risk for MetS. This thesis includes two independent research studies investigating the effect of carbohydrate source and a HPD on markers of MetS. Collectively, the results misalign with the central hypothesis and suggest that carbohydrate source with a HPD will not significantly affect markers of MetS in adults at risk for MetS.

Study 1, a randomized control trial, was designed to evaluate the effect of a higher protein test breakfast containing white potatoes or a control carbohydrate (white rice) on appetite, palatability, and postprandial glucose and insulin concentrations on 23 adult men and women at risk for MetS. To our knowledge, this is the first study to examine the role of the carbohydrate source with a higher protein test breakfast on markers of metabolic syndrome in adults at risk for MetS. The present study tested the hypothesis that HPD containing white potatoes will improve markers of MetS in adults at risk for MetS. Our results indicate that a higher protein test breakfast containing white potatoes does not lead to significant changes in appetite, palatability, or plasma biomarkers within 240 minutes of test breakfast consumption when compared to a higher protein test breakfast containing white rice. Collectively, this data suggests that in adults at risk of MetS, consumption of white potatoes with a HPD will not negatively impact markers of MetS when compared to a control carbohydrate. However,

beyond the test breakfast, no other form of dietary assessment was performed. This could have been a contributing factor in the lack of measured significant effects between the dietary treatment groups. Therefore, future research should focus on whether consumption of a higher protein test breakfast containing white potatoes has similar effects on ad libitum food intake following test breakfast consumption compared to a higher protein test breakfast containing a control carbohydrate (white rice).

Study 2, a 16-week randomized control trial, was designed to investigate the effects of long-term consumption of a HPD containing white potatoes on body composition and cardiometabolic biomarkers of MetS in 21 adult men and women at risk for MetS. To our knowledge, this is the first study to examine the effects of consumption of a HPD with white potatoes or a control carbohydrate (white rice/pasta) on markers of metabolic syndrome in a state of weight maintenance in adults at risk for MetS. The present study tested the hypothesis that a HPD containing white potatoes will improve body composition and cardiometabolic biomarkers in adults at risk for MetS. Our results indicate that a HPD containing white potatoes does lead to significant changes in body composition and cholesterol, but not other cardiometabolic biomarkers when compared to a HPD containing a control carbohydrate (white rice/pasta). Collectively, this data suggests that in adults at risk of MetS there is potential for carbohydrate source to be useful in the treatment of markers of MetS. Perhaps the most influential of the limitations of the current study is the incongruence between the prescribed macronutrient ratio and the macronutrient ratio that the participants actually consumed. Each participant was instructed to follow a macronutrient ratio of 30% protein, 30% fat, and 40% carbohydrates, however, the HPWP group consumed 19.1% protein, 38.9% carbohydrates, and

42.6% fat, while the HPCC consumed 17.7% protein, 45.6% carbohydrates, and 36.6% fat. Indeed, it is common to encounter underreporting of dietary intake in many nutritional studies, especially in those relating diet to obesity or obesity-related disorders [336]. However, the question still arises whether the results of the current study can truly be related to HPDs. It is true that the actual protein consumption for both the HPWP and HPCC groups was lower than prescribed, however, according to the Centers for Disease Control and Prevention, the average protein intake among adults aged 20 and over was 15.8% as of 2018 [337]. Therefore, participants in the current study were still consistently consuming greater-than-average amounts of protein, and results may still be applicable to higher protein intake. Regardless, this could have been a contributing factor in the lack of improvement in cardiometabolic biomarkers between the dietary treatment groups. Future research should focus on whether consumption of a strict HPD containing white potatoes shows improvement in cardiometabolic biomarkers of MetS compared to a HPD containing a control carbohydrate (white rice/pasta).

Collectively, the results of this thesis suggest that consumption of a HPD containing white potatoes will not affect markers of MetS. However, there is potential for carbohydrate source to be useful in the treatment of markers of MetS. Additional research is necessary to validate these findings.

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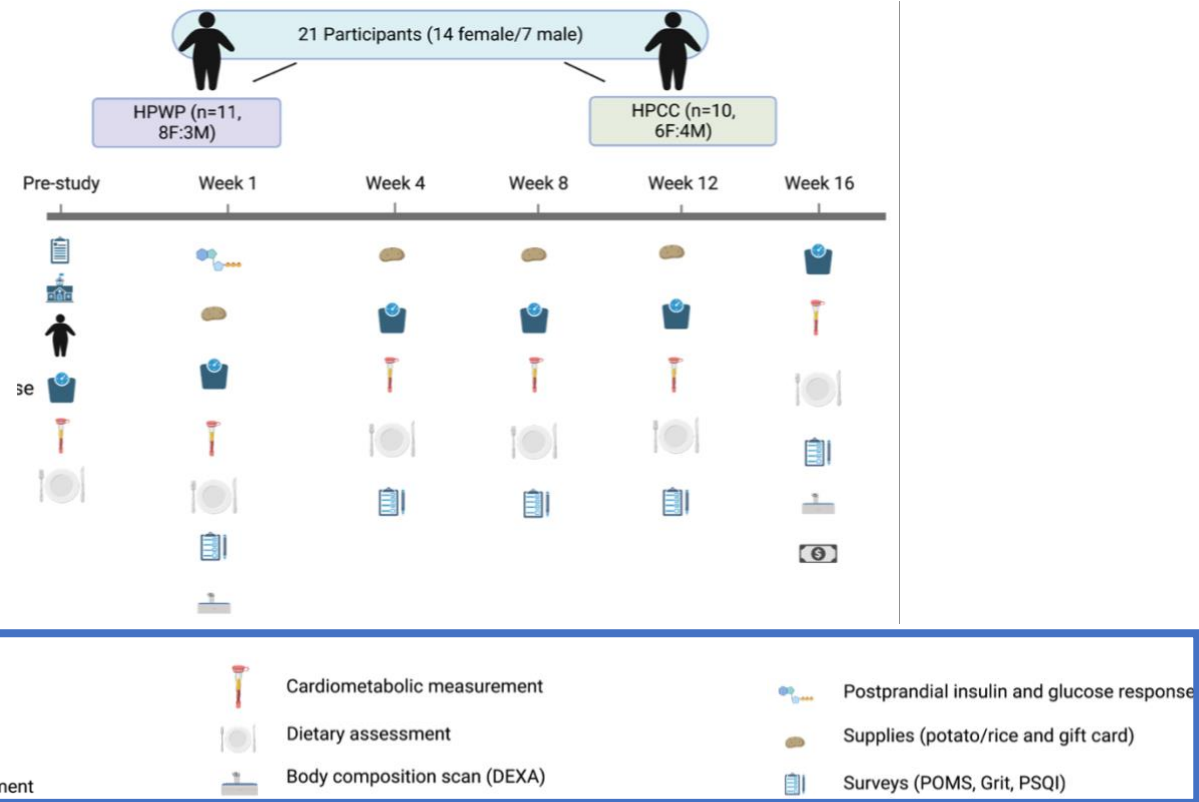
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Appendix

Appendix 1. Inclusion and exclusion criteria.

| Inclusion | Exclusion |
|--|--|
| Over 18 years of age | Prescription medications |
| Men and women | Food allergies |
| Resident of Northwest Arkansas | Pregnant or lactating women |
| Two or more characteristics of Metabolic Syndrome | Dietary restrictions |
| <ul style="list-style-type: none"> - BMI greater than 25 - Abdominal obesity (waist to hip ratio: ≥ 0.90 in men, ≥ 0.85 in women) - Triglyceride >150 mg/dL - HDL cholesterol < 40 mg/dL in men, < 50 mg/dL in women - Systolic blood pressure > 130 mm Hg - Diastolic blood pressure > 85 mm Hg and/or - Fasting glucose > 100 mg/dL | Fear of needles Chronic mental health problems (anxiety, depression) Greater than 5% loss of body weight in past three months Currently consuming a higher protein diet |

Appendix 2. Schematic representation of study design.



Appendix 3. Average amino acid intake of adults at risk of MetS over 16-week dietary intervention¹

| | Time (weeks) | | | |
|------------------------|--------------|-------------|-------------|--------------|
| | 0 | 8 | 16 | Δ |
| Amino acid content (g) | | | | |
| Tryptophan | | | | |
| HPCC | 3.21 ± 1.34 | 3.26 ± 1.03 | 3.11 ± 0.85 | -0.09 ± 0.07 |
| HPWP | 1.54 ± 1.40 | 1.62 ± 0.85 | 1.29 ± 0.47 | -0.25 ± 0.18 |
| Threonine | | | | |
| HPCC | 3.70 ± 1.51 | 3.78 ± 1.14 | 3.55 ± 0.90 | -0.15 ± 0.11 |
| HPWP | 2.35 ± 1.71 | 2.75 ± 2.24 | 2.66 ± 2.17 | 0.31 ± 0.22 |
| Isoleucine | | | | |
| HPCC | 6.31 ± 2.60 | 6.40 ± 2.06 | 6.11 ± 1.69 | -0.20 ± 0.14 |
| HPWP | 2.61 ± 2.18 | 3.04 ± 2.76 | 2.99 ± 2.65 | 0.38 ± 0.28 |
| Leucine | | | | |
| HPCC | 5.47 ± 2.33 | 5.63 ± 1.77 | 5.22 ± 1.64 | -0.26 ± 0.18 |
| HPWP | 4.33 ± 3.66 | 5.03 ± 4.64 | 4.82 ± 4.33 | 0.49 ± 0.35 |
| Lysine | | | | |
| HPCC | 1.90 ± 0.83 | 1.89 ± 0.57 | 1.76 ± 0.35 | -0.15 ± 0.10 |
| HPWP | 4.23 ± 2.99 | 5.19 ± 4.22 | 4.78 ± 3.87 | 0.55 ± 0.39 |
| Methionine | | | | |
| HPCC | 1.09 ± 0.42 | 1.13 ± 0.35 | 1.05 ± 0.31 | -0.03 ± 0.02 |
| HPWP | 2.30 ± 0.82 | 2.70 ± 0.84 | 2.57 ± 0.82 | 0.27 ± 0.19 |

Appendix 3 continued. Average amino acid intake of adults at risk of MetS over 16-week dietary intervention¹

| | Time (weeks) | | | |
|------------------------|--------------|-------------|-------------|--------------|
| | 0 | 8 | 16 | Δ |
| Amino acid content (g) | | | | |
| Cystine | | | | |
| HPCC | 3.60 ± 1.46 | 3.57 ± 1.03 | 3.36 ± 0.73 | -0.24 ± 0.17 |
| HPWP | 1.89 ± 1.25 | 2.13 ± 1.20 | 2.16 ± 1.14 | 0.27 ± 0.19 |
| Phenylalanine | | | | |
| HPCC | 2.85 ± 1.20 | 2.77 ± 0.86 | 2.60 ± 0.55 | -0.25 ± 0.18 |
| HPWP | 4.35 ± 1.59 | 4.84 ± 1.56 | 4.72 ± 1.47 | 0.37 ± 0.26 |
| Tyrosine | | | | |
| HPCC | 4.10 ± 1.65 | 4.16 ± 1.24 | 3.86 ± 0.95 | -0.24 ± 0.17 |
| HPWP | 3.51 ± 1.37 | 4.24 ± 1.54 | 4.10 ± 1.40 | 0.59 ± 0.42 |
| Valine | | | | |
| HPCC | 4.41 ± 1.86 | 4.65 ± 1.34 | 4.27 ± 1.16 | -0.15 ± 0.10 |
| HPWP | 3.47 ± 1.77 | 3.97 ± 2.28 | 3.82 ± 2.09 | 0.35 ± 0.25 |
| Arginine | | | | |
| HPCC | 2.26 ± 0.93 | 2.25 ± 0.64 | 2.10 ± 0.47 | -0.17 ± 0.12 |
| HPWP | 3.53 ± 2.38 | 4.12 ± 3.09 | 3.88 ± 2.80 | 0.35 ± 0.25 |
| Histidine | | | | |
| HPCC | 3.95 ± 1.65 | 4.07 ± 1.18 | 3.79 ± 0.94 | -0.15 ± 0.11 |
| HPWP | 2.69 ± 0.91 | 2.99 ± 0.99 | 3.05 ± 0.88 | 0.36 ± 0.26 |

Appendix 3 continued. Average amino acid intake of adults at risk of MetS over 16-week dietary intervention¹

| | Time (weeks) | | | |
|------------------------|--------------|--------------|--------------|--------------|
| | 0 | 8 | 16 | Δ |
| Amino acid content (g) | | | | |
| Alanine | | | | |
| HPCC | 7.19 ± 2.82 | 7.34 ± 2.26 | 6.84 ± 2.11 | -0.34 ± 0.24 |
| HPWP | 3.70 ± 1.54 | 4.20 ± 2.01 | 4.26 ± 1.97 | 0.57 ± 0.40 |
| Aspartic acid | | | | |
| HPCC | 15.98 ± 6.66 | 15.01 ± 4.89 | 14.80 ± 3.67 | -1.18 ± 0.84 |
| HPWP | 6.51 ± 3.13 | 7.56 ± 4.03 | 7.24 ± 3.76 | 0.74 ± 0.52 |
| Glutamic acid | | | | |
| HPCC | 3.56 ± 1.53 | 3.59 ± 1.01 | 3.32 ± 0.75 | -0.24 ± 0.17 |
| HPWP | 11.77 ± 7.16 | 12.75 ± 8.33 | 11.79 ± 7.58 | 0.02 ± 0.01 |
| Glycine | | | | |
| HPCC | 5.41 ± 2.43 | 4.86 ± 1.64 | 4.93 ± 1.11 | -0.49 ± 0.34 |
| HPWP | 3.27 ± 1.55 | 3.67 ± 1.82 | 3.63 ± 1.75 | 0.36 ± 0.25 |
| Proline | | | | |
| HPCC | 3.64 ± 1.47 | 3.68 ± 1.12 | 3.45 ± 0.94 | -0.19 ± 0.13 |
| HPWP | 4.59 ± 1.71 | 5.02 ± 1.94 | 4.71 ± 1.64 | 0.11 ± 0.08 |
| Serine | | | | |
| HPCC | 3.21 ± 5.49 | 1.76 ± 3.09 | 0.90 ± 1.27 | -2.31 ± 1.63 |
| HPWP | 4.63 ± 1.97 | 5.44 ± 2.03 | 5.18 ± 1.81 | 0.54 ± 0.39 |

¹Values are mean ± SD. HPWP, high protein white potato, n=11; HPCC, high protein control carbohydrate, n=10.

Appendix 4. IRB approval letter



To: Jamie I Baum
FDSC N2216

From: Douglas James Adams, Chair
IRB Committee

Date: 03/05/2019

Action: **Approval**

Action Date: 03/05/2019

Protocol #: 1901172168

Study Title: Diet and Health in Adults with Metabolic Syndrome

Expiration Date: 02/12/2020

Last Approval Date:

Risk Level:

The above-referenced protocol has been approved following Full Board Review by the IRB Committee that oversees research with human subjects.

If the research involves collaboration with another institution then the research cannot commence until the Committee receives written notification of approval from the collaborating institution's IRB.

It is the Principal Investigator's responsibility to obtain review and continued approval before the expiration date.

Protocols are approved for a maximum period of one year. You may not continue any research activity beyond the expiration date without Committee approval. Please submit continuation requests early enough to allow sufficient time for review. Failure to receive approval for continuation before the expiration date will result in the automatic suspension of the approval of this protocol. Information collected following suspension is unapproved research and cannot be reported or published as research data. If you do not wish continued approval, please notify the Committee of the study closure.

Adverse Events: Any serious or unexpected adverse event must be reported to the IRB Committee within 48 hours. All other adverse events should be reported within 10 working days.

Amendments: If you wish to change any aspect of this study, such as the procedures, the consent forms, study personnel, or number of participants, please submit an amendment to the IRB. All changes must be approved by the IRB Committee before they can be initiated.

You must maintain a research file for at least 3 years after completion of the study. This file should include all correspondence with the IRB Committee, original signed consent forms, and study data.

cc: Aubree L Worden, Key Personnel
Hexirui Wu, Key Personnel
Angela M Tacinelli, Key Personnel
Drake Palmer Enderlin, Key Personnel
McKenzie Jayne Fellingner, Key Personnel
Samuel Preston Belt Walker, Key Personnel