THE UTILITY OF ALTERNATIVE BODY COMPOSITION MEASURES TO ASSESS BODY FATNESS AND CARDIOMETABOLIC RISK IN FEMALE COLLEGE STUDENTS

by

MEYNARD JOHN L. TOLEDO

(Under the Direction of Michael Schmidt)

ABSTRACT

This study sought to determine which anthropometric measure (body mass index (BMI), waist circumference (WC), waist circumference-to-height ratio (WHtR), or a body shape index (ABSI)) best predicts fatness and cardiometabolic risk (CMR) and how using different fatness measures affect the association between physical activity (PA) and CMR score. Anthropometric measures, dual energy X-ray absorptiometry (DXA) (GE iLunar) measures, PA via accelerometers (NL-1000), and CMR profile from 334 college females were analyzed. WHtR best predicted central (r=.84) and total body fat (r=.80). Body fat measures were weakly to moderately correlated with CMR profile (r of 0 to .59). PA's association with overall CMR ranged from standardized beta coefficient of -0.44 to -0.79. WHtR, WC, and BMI could serve as surrogate measures for body fatness in college females. No single fat measure best predicted all CMR factors. However, the choice of adiposity measure affects the strength of association between PA and CMR.

INDEX WORDS: anthropometric measures; predictors of body fat; predictors of cardiometabolic risk; physical activity and cardiometabolic risk

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DEDICATION

This thesis is dedicated to my family and friends who have continuously been in my side, supporting and encouraging me throughout this process. Your constant support helped me realize my potential and succeed in my endeavors. Without you, this journey would have been dull and dreary.

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CHAPTER 1

INTRODUCTION

Obesity is a major public health problem in the U.S. where more than 33% of adults are obese [16]. This is more than double the rate of obesity 50 years ago[15]. Furthermore, data from the National College Health Risk Behavior Survey indicate that 35% of college-aged students are overweight or obese [12]. This is alarming considering that overweight and obesity leads to an array of elevated risk factors and diseases such as type 2 diabetes mellitus and cardiovascular disease (CVD) [6, 11]. Moreover, the economic burden of obesity is tremendous. In the US alone, the direct cost of obesity is estimated to be $113.9 billion [20].

Previous research shows that different metabolic abnormalities that occur with obesity can cluster together in many individuals. For example, one study showed that obesity can be accompanied by metabolic abnormalities such as hypertension and dyslipidemia, ultimately leading to CVD [18]. Cardiometabolic risk (CMR) is an umbrella term for different risk factors that contribute to the development of CVD and type 2 diabetes mellitus. It includes traditional and emerging risk factors such as obesity, insulin resistance, hyperglycemia, dyslipidemia, hypertension, smoking habits, physical inactivity, and unhealthy diet [10]. One subset of CMR which has been a focus of current studies is metabolic syndrome (MetS). It encompasses a limited number of risk factors linked to insulin resistance and is associated with visceral fat deposition along with abnormalities in blood glucose, blood pressure (BP), triglycerides (TRG), and/or high-density lipoprotein cholesterol (HDL-C) [10]. Current studies indicate that 7-12% of college students meet the criteria for MetS and 30-40% exhibit at least one indicator of this

condition [2, 9, 19]. In addition, obese college students have been shown to have three times the risk of developing at least one CMR indicator [7], reflecting the strong contribution of body fatness to CMR.

Currently, dual energy X-ray absorptiometry (DXA) is the most available and accurate means for estimating body composition [13] but the technology is expensive and impractical to use for screening in larger populations. An alternative for body composition measurement is the use of anthropometric measures like body mass index (BMI), waist circumference (WC), and waist circumference-to-height ratio (WHtR). These measures have also been shown to correlate with CMR. Westphal et al observed that BMI, WC, and WHtR are good predictors of different metabolic risk indicators (uric acid, TRG, cholesterol, HDL-C, C-reactive protein (CRP), systolic BP, and insulin resistance (HOMA-IR) in 28-84-year-old adults [1]. Furthermore, WC has been shown to be more strongly correlated with CMR than BMI among adults, presumably because WC is a better indicator of visceral adiposity which is highly associated with an adverse metabolic profile [17]. However, few studies have directly compared the utility of commonly used anthropometric indices to predict CMR in college-aged females. In a cross-sectional study by Morrel et al where they characterized the prevalence and relationship of obesity and metabolic syndrome indicators, they observed that college students with BMI greater than 30 meet 1-2 more MetS criteria, based on the ATP III report [5], compared to students with normal BMI [14].

Regular physical activity (PA) of at least moderate intensity has been shown to improve MetS and reduce CMR in general population samples [3, 4, 8, 21]. However, the results of studies that have explored the extent to which PA is associated with reduced CMR independent of body fatness have been conflicting. In a cross-sectional study of children (9 years, n = 273)

and adolescents (15 years, n = 256), PA was not significantly correlated with a summary CMR score, computed as the mean of the standardized outcome scores of fasting insulin, glucose, TRG, total cholesterol, HDL-C, and BP, when adjusted by adiposity. In contrast, a meta-analysis of 14 studies that looked at the independent and combined associations between objectively measured time in moderate- to vigorous-intensity physical activity (MVPA) and sedentary time with CMR factors in children (aged 4-18 years) revealed that MVPA is inversely associated with TRG (β-coefficient = -.017, *95% CI* -.025 to -.009) and fasting insulin (β-coefficient = -.028, *95% CI* -.038 to -.017) even after adjustment for waist circumference [3]. While the earlier study adjusted their results by body fatness, the later adjusted their results using WC as a measure of body fatness. This difference in measures used to estimate body fatness across studies provides a plausible explanation for these inconsistent findings.

Currently, numerous studies are being conducted to answer questions pertaining to obesity, CMR, and its impact on the health of the public but the differences of methods, especially the lack of uniformity in the anthropometric measure used to estimate body fatness, tends to limit our ability to make conclusions on these topics. Future research needs to identify the best indicator of metabolic risk in different populations, especially emerging adults, to aid our understanding how adjustments for different body composition measures can influence the observed association between PA and CMR. Determining which anthropometric measure (BMI, WC, or WHtR) is the best predictor of body fatness and CMR factors, and to determine their possible effect on the relationship of PA and CMR among college aged- females is a step towards this goal.

Statement of the Problem

This study aims to determine which anthropometric measure (BMI, WC, or WHtR) is the best indicator of total and central body fat measured by DXA scan in college-aged females. Furthermore, we intend to identify which anthropometric measure is most strongly correlated with CMR, such as plasma levels of TRG, HDL, low density lipoprotein (LDL), HOMA-IR, and CRP, and to characterize the nature of its relationship. Lastly, we aim to examine the extent to which the choice of body composition measure may affect observed associations with cardiometabolic disease risk independent of PA.

Specific aim #1. To determine the extent to which BMI, WC, WHtR, and ABSI predict DXA measured total and central body fat in college-aged females.

Hypothesis #1. BMI will be a better predictor of total body fat while WC will be more accurate in predicting central body fat.

Specific aim #2. To determine which measure of body composition is most strongly correlated with CMR in college-aged females.

Hypothesis #2. The correlation between body fatness and CMR will vary depending on which measure of body fatness is used. WC will exhibit the highest association with CMR with BMI and WHtR l also demonstrating modest associations.

Specific aim #3. To examine the extent to which different methods of body composition measurement influence the strength of association between PA and CMR in college-aged females.

Hypothesis #3. Associations between PA and CMR indicators will be strongest when WC or WHtR is used as the measure of body composition compared to BMI.

Significance of the Study

This study provides future researchers with evidence of the relative validity of different anthropometric measures in estimating body fatness and CMR in college-aged females to inform future population-based studies and perhaps influence clinical practice. In addition, the study also provides information as to how different measures of body fatness affect the relationship between PA and CMR. These results could potentially explain the conflicting results from different studies examining the relation between PA and CMR. Thus, future researchers can be guided on what anthropometric measure of body fatness should be used in determining the independent effect of PA on CMR.

As this study determined the best surrogate measure of body fatness and CMR among college females, college students and health practitioners, specifically those who are working with this specific group, will be better informed as to which anthropometric measure to use to assess body fat level and risk for cardiometabolic disease. Students with high CMR could be easily identified, leading to earlier health intervention. Furthermore, with proper education and information dissemination, students will be more aware of their health status and risks.

Scope, Limitations, and Delimitations

The data used in the study was from the POWER DAWGS and SPIN DAWGS studies which involved approximately 500 college-aged females from the University of Georgia, Athens (UGA). Unlike other studies on this topic, this study looked at general CMR factors of students and not metabolic syndrome alone. To asses for CMR factors, plasma analysis for lipid profile (HDL-C, LDL, and TRG), glucose and insulin, and CRP was conducted through a nationally certified lab (Quest Diagnostics). WC, weight, and height were obtained by trained personnel to calculate WHtR and BMI. DXA scans were also obtained as a measure of total and regional

body fatness. New-Lifestyle-1000 accelerometers were used to assess 7-day PA levels of each subject.

Due to factors outside the control of the researcher, the following are the limitations of the study:

1. Because of the diversity of students in UGA, generalizability of results may only be applicable to female students of this university. Results may not be applicable to the general college–aged population in the country.
2. Because subjects are college-aged females that are mostly healthy, plasma analysis of CMR factors were mostly within normal range which limited the study's ability to evaluate associations between risk factors and anthropometric measures.
3. Physical activities of the subjects were measured using the NL-1000 accelerometers which only give steps per day or activity minutes per day. This limited the ability of the researcher to manipulate data for deeper analysis (e.g. sedentary time). In addition, differences in wear time lengths could affect comparability of data between subjects. Like other accelerometers, water activities and PAs that does not involve hip movement such as upper body exercises and biking, were not recorded.

Assumptions

In this study, various assumptions about the subjects were made. First, during assessment of CMR, the subjects were expected to follow any fasting protocol as directed before the scheduled blood draw. Failing to do so could alter the results of the test which could significantly impact the analysis. Second, it was also assumed that accurate anthropometric measures were obtained by the laboratory personnel. Proper training was conducted to assure accuracy in obtaining these measurements. Third, it was assumed that the measured PA of the subjects reflects their habitual PA and that they did not alter their behavior when wearing our

measurement device. If measured PA was not their habitual PA, any associations seen in the analysis were of limited validity.

Definition of Terms

To avoid confusion and facilitate better understanding of the study, the following terms were defined operationally:

1. Anthropometric Measurement indicates the non-invasive measurement of body weight, height, waist circumference aimed at estimating body fatness or body fat distribution.
2. Body Fatness is the measurement of how much of a person's total body weight is attributed to fat mass expressed as a percentage. In this study, fat mass was measured via DXA and will be used as the reference value. Both central and total fat mass will be evaluated and compared to the anthropometric measures.
3. Body Mass Index is the ratio of a person's weight to height expressed in kg/m^2.
4. Cardiometabolic Risk was measured using systolic blood pressure and plasma analysis of the subject's lipid profile, glucose and insulin, and CRP. The sum of the z-score of these measures was calculated to estimate overall CMR.
5. Physical activity refers to all activities of a subject recorded by the NL-1000 accelerometer throughout the entire 7 days. Physical activity was be expressed in total number of minutes of physical activity per day (average active minutes/day).
6. Waist Circumference refers to the perimeter of the narrowest (WC-N) part between the subject's iliac crest and lowest rib measured in centimeter. A second measurement was also taken at the level of the umbilicus (WC-U).
7. Waist circumference-Height Ratio refers to the ratio of the subject's WC-N to her height.

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CHAPTER 2

REVIEW OF RELATED LITERATURE

The current obesity epidemic is very alarming considering its health and economic impact. A survey in 2012 showed that more than 33% of adults in the United States are obese and that another 30% are overweight [46]. Furthermore, this number is also increasing in younger populations. Data from the National Health and Nutrition Examination Survey (NHANES) showed that 17% of children and adolescents aged 2-19 years are obese [47]. In addition, the National College Health Risk Behavior Survey indicated that 35% of college students are overweight or obese [42]. The prevalence of obesity in the general population is disturbing considering the significant amount of evidence that links obesity to various cardiometabolic abnormalities such as diabetes mellitus type 2 and cardiovascular disease (CVD) [22, 41].

Measuring Obesity

Generally, the human body can be quantified at several levels: at an atomic level by quantifying the amount of basic elements present in the body like oxygen, carbon, hydrogen, nitrogen, and other trace elements; at the molecular level by amounts of water, lipid, protein, and carbohydrates; at the cellular level by extracellular fluids and body cell mass; and at a tissue level by the amounts and distribution of skeletal, muscle, and adipose tissues [15]. The atomic to the cellular level can be assessed by direct body composition methods like neutron activation, isotope dilution and total body counting [15]. On the other hand, criterion measures of body composition evaluate specific properties such as body density or the amount and distribution of

tissues. Densitometry, dual energy X-ray absorptiometry (DXA), computed X-ray tomography (CT-scan), and magnetic resonance imaging (MRI) are classified under this category. The indirect method, which includes anthropometry and bioelectrical impedance analysis, provides an estimate of body composition based on biological relationships between direct and criterion measures of body component and tissue distributions among normal individuals [15].

Obesity is defined as the degree of excess fat mass that is associated with elevated health risk. In 1993, the *World Health Organization Expert Committee on Physical Status: The Use and Interpretation of Anthropometry* met in Geneva to review existing literature on the use of anthropometric measurements as determinants of an individual's health risk. Despite having more accurate measures of body fatness like skinfold thickness and underwater weighing available at that time, they proposed different cutoff points for BMI (25, 30, and 40) as the criterion to identify individuals that are overweight, obese, and morbidly obese [1] because of its practicality. Since these BMI cutoff points are an index of one's risk for morbidity and mortality based on weight and height and not necessarily of body fatness, there is a significant portion of the population that are misclassified using this measure [2, 30, 57]. In one study, the authors evaluated the accuracy of BMI in identifying individuals that are obese by comparing it with percent body fat measured by air displacement plethysmography using 25% and 35% body fat as the cutoff points for obese men and women respectively. They found that 8% of men and 7% of women were incorrectly classified as obese and 41% of men and 32% of women have false-negative results when using the standard BMI cutoff points [57]. This means that 41% of men and 32% of women have been misclassified as either normal weight or overweight despite having a body fat percentage high enough to be considered obese.

Current advances in technology have allowed researchers to utilize various techniques such as DXA and air displacement plethysmography which offer a relatively accurate measure of total body fatness [43]. However, these techniques needs specialized personnel training and are expensive to operate which makes them impractical for use in population-based screening and research. Other measures of body fatness are also available such as bioelectrical impedance analysis (BIA), a method that is more affordable and more feasible in population-based studies. Notably, BIA makes use of impedance index to estimate total body water, which is an independent predictor of an individual's body composition; although it has more error than DXA [15]. Despite these measures, there is still no consensus among experts as to the percent body fat cutoff points that will classify an individual as being overweight or obese.

Obesity and Cardiometabolic Risk

Although viewed as a negative trait and a major risk factor of various cardiometabolic diseases in today's society, being obese did not always carry this stigma. In fact, people in the past viewed obesity as a sign of good health and vitality. Perhaps one of the earliest proofs of this concept is the discovery of 20,000 year-old stone figures in Willendorf, Austria in 1908. These stone figures, which are believed to be the matriarchal icons of fertility, depict nude female figures showing bulbous contours and prominent belly [17]. In addition, the medical society used to advocate that carrying extra amounts of "flesh" of about 20-50 pounds was healthy because it provides extra energy during periods of prolonged illness [49].

One of the earliest studies to provide evidence regarding the health risks of obesity was published in the 1920's by Dr. Louis Dublin when he analyzed data on policy stakeholders of the Metropolitan Life Insurance Company and reported evidence of differential mortality by weight and its association with specific diseases [14]. By the 1930's, physicians started to advocate

against obesity and overeating practices to promote healthier weight levels. At the same time, research related to obesity started to increase. By the 1960's, advances in the field of physiology led researchers to consider adipose tissues as an active organ with receptors, genetics, cellular biology mechanisms, and hormones and not just passive fat storage units [17]. Currently, there is a wealth of evidence that links obesity with increased risk of all-cause mortality [18, 19, 38, 64]. For example, a meta-analysis of 97 studies with a combined sample size of 2.88 million including 270,000 deaths showed that obese individuals, when compared to normal weight individuals, have a higher incidence of all-cause mortality (Hazard Ratio 1.18, 95% CI 1.12-1.25) for all grades of obesity combined [19].

In addition to this higher mortality risk, obesity has also been associated with a higher incidence of cardiometabolic diseases. Cardiometabolic risk (CMR) is an umbrella term for different risk factors that contribute to the development of CVD and type 2 diabetes mellitus. It includes traditional and emerging risk factors such as obesity, insulin resistance, hyperglycemia, dyslipidemia, hypertension, smoking habits, physical inactivity, and unhealthy diet [40]. One subset of CMR factors which has been the focus of substantial research is known as the metabolic syndrome (MetS). This syndrome refers to the clustering of three or more risk factors linked to insulin resistance including visceral fat deposition and elevated levels of blood glucose, blood pressure (BP), triglycerides (TRG), and/or high-density lipoprotein cholesterol (HDL-C) [40]. Current studies indicate that 7-12% of college students meet the criteria for metabolic syndrome and 30-40% exhibit at least one indicator of this condition [9, 33, 62]. In addition, obese college students have been shown to have three times the risk of developing at least one CMR indicator [26], reflecting the strong contribution of body fatness to CMR.

Glucose Control

There is a high correlation between obesity and diabetes risk. In fact, it is estimated that 60% of diabetes mellitus cases are related to obesity [48]. A study in 2005 of 87 women (40 obese and 47 non-obese) aged 50-64 years old revealed that insulin resistance (homeostatic model assessment of insulin resistance (HOMA-IR)) in obese individuals is significantly higher compared to their non-obese counterparts (mean±SD of 3.38±2.64 vs 1.20±0.73, $p<.001$) [13]. In addition, childhood obesity seems to be a good predictor of diabetes risk during adulthood. One study retrospectively looked at the childhood weight status of 240, 32-38 year-old, overweight adults with abnormal glucose and/or lipid profiles and showed that being overweight or obese at age 13-15 increases a person's risk of developing abnormal glucose level ($OR \geq 8.6$, $p<.001$) [52]. Furthermore, a review of the long term (>2 years) effect of weight loss on risk for diabetes indicated that those who lost minimal weight (3-5 kg) and maintained it have a reduced risk of developing diabetes (RR=0.68, CI 0.59-0.80).

A number of mechanisms have been proposed to explain how obesity could lead to diabetes mellitus. For example, free fatty acids, which are usually increased with fat mass expansion, could serve as signaling molecules that activate protein kinases. These kinases increase inhibitory serine phosphorylation of insulin receptor substrates, the key mediator of insulin receptor signaling [50]. Systemic inflammation has also been linked to the development of insulin resistance [24] and various molecules, systems, and pathways have been shown to have potential links to insulin resistance. Multiple endocrine, inflammatory, and neural pathways are altered in situations of excess fat mass in the body which could further lead to modulation of various signaling pathways that are cell-intrinsic and functional in various metabolic tissue including fat, liver, and muscles [55]. Although it is possible that one of these factors could serve

as the main mechanism that leads to insulin resistance, it is more likely that the interplay between these interdependent factors explains the pathophysiology of how obesity leads to insulin resistance [55].

Lipid Profile

Obesity also has strong associations with abnormal triglyceride levels. Data from the *National Health and Nutrition Examination Survey* (NHANES) revealed that triglyceride level increases with increasing obesity level in white men and women of all ages. Researchers found that triglyceride levels of obese individuals (BMI>30 kg/m^2) were higher by 100 mg/dl in males and 60 mg/dl in females when compared to those who have normal weight (BMI<25 kg/ m^2) [10, 11]. These results are corroborated by data from the Coronary Risk Development in Young Adults (CARDIA) study where they looked at longitudinal data on the relationships of lifestyle and physiological variables to the development of coronary heart disease risk factors in 1,777 men and women aged 18-30 years old. They noted that weight increase is accompanied by increasing levels of plasma triglycerides [61].

Another lipid measure that has been strongly correlated with obesity is plasma high density lipoprotein cholesterol (HDL-C) level. NHANES data suggest a 10 mg/dl difference in HDL-C levels among normal versus obese men and that this difference may be greater in women [10, 11]. Regression analysis from the CARDIA study showed that for every 1 unit increase in BMI, plasma HDL-C level drops by approximately 3 mg/dl [61]. To support this, a review of weight loss intervention studies revealed that weight loss is consistently accompanied by a subsequent increase in plasma HDL-C level [25].

Despite this evidence illustrating the association of plasma triglyceride and HDL-C level with obesity, evidence linking plasma low density lipoprotein cholesterol (LDL-C) level with

obesity is not clear. Cross sectional analysis [10, 11] of the NHANES data of young (20-44 years old) men and women showed a significantly higher level of LDL-C (difference of 30 mg/dl and 20 mg/dl, respectively) in obese individuals compared to those who have normal weight. In contrast, BMI was observed to have a minimal effect on LDL-C level of middle-aged men and women (45-59 years old). Data from longitudinal studies show that LDL-C levels rise with weight and that for every 1 unit increase in BMI, LDL-C level increases by 5.5 mg/dl [3, 59]. Despite these findings from longitudinal studies, results of various long-term weight loss studies are less consistent with some studies reporting significant decreases in LDL-C level with weight loss [15, 65, 66] and some reporting no change [29, 32, 44].

Just like the relationship of obesity and insulin resistance, the pathophysiology of the typical dyslipidemia observed in obesity is multifaceted and involves various processes. Hypertriglyceridemia may be the primary cause of other lipid abnormalities since it leads to delayed clearance of TRG rich lipoproteins [36, 37]. This leads to a series of processes that includes hepatic overproduction of VLDL, decreased circulating TRG lipolysis and impaired peripheral FFA trapping, increased FFA fluxes from adipocytes to the liver and other tissues and the formation of small dense LDL [37]. All of these contribute to the abnormality in lipid profile of an obese individual.

Blood Pressure

Blood pressure is another risk factor that is strongly linked with obesity. In fact, data from the Framingham Heart study showed that obesity accounts for 78% and 68% of essential hypertension cases in men and women, respectively [31]. Cross sectional analysis of the NHANES data revealed that the prevalence of hypertension in obese individuals is 1.8 times greater in men and 1.5 times greater in women when compared to normal weight individuals

[53]. In addition, data from the Nurses' Health study which involved 80,000 women revealed that a 5 kg weight gain after the age of 18 years results in a 60% higher relative risk of developing hypertension and that a 10 kg weight gain would increase one's risk by 2.2 times [27]. Various physiological factors that potentially link obesity to hypertension include hyperinsulinemia, hyperleptinemia, renal dysfunction, altered vascular structure and function, enhanced sympathetic and renin-aldosterone-angiotensin system activity, and blunted natriuretic peptide activity [4].

Predictors of cardiometabolic risk

With advances in obesity research, investigators started to notice that a centralized fat pattern is associated with intra-abdominal fat deposition which is also highly related to CMR. The development of specialized imaging techniques to measure fat mass as CT, MRI, and DXA methods enabled researchers to look at specific body fat compartments and their relationship with different CMR factors [20]. Specifically, in both men and women, a standard deviation increase in visceral fat compartment was more strongly associated with an increased risk for MetS than the same degree of increase in subcutaneous fat (OR of 4.2-4.7 vs 2.5-3.0, $p<.0001$).[20].

Although methods that explore these different compartments are available, the practicality of their use in larger studies is still an issue. Notably, BMI has been shown to be inaccurate at estimating abdominal fatness [5, 20, 30, 57]. To address this problem, measures such as waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) were developed to act as surrogate measures of abdominal fat for better CMR assessment.

One of the earliest measures developed to estimate abdominal fatness that was highly correlated with CMR factors was WC. Because WC is a simple anthropometric measure of

abdominal girth, it should be noted that this measure includes both visceral (VAT) and subcutaneous (SAT) adipose tissues [15]. In a study of 1,667 men and women of both African-American and Caucasian descent, they found that WC is more strongly correlated with abdominal SAT (r=.82-.92, p<.001) than VAT (r=.73-.77, p<.001) [8]. Nevertheless, studies have shown that WC is more strongly correlated with CMR than BMI among adults [5, 35, 60]. Using regression analysis from BMI of Caucasian men and women in Glasgow, Scotland, WC cutoff points (WC>102 cm in men and WC>88 cm in women) that are highly associated with increased risk for cardiometabolic diseases were identified [39] . Different organizations such as the National Heart, Lung, and Blood Institute, Shaping America's Health: Association for Weight and Obesity Prevention, The Obesity Society, and American Diabetes Association support the use of WC as a clinical tool to assess CMR [35].

The ratio of WC to hip circumference is another simple measure that is useful for determining abdominal fat accumulation patterns [15]. One advantage of using WHR is that it accounts for differences in body structure. Thus, two people having the same WHR could have very different waist and hip measurements. WHR has been found to be accurate in predicting mortality [54] and cardiovascular disease risk [45] but is less capable of predicting CMR factors than WC [12, 34, 51].

Recently, the ratio of a person's WC to height (WHtR) has been used to measure patterns of body fat distribution. One advantage of WHtR is that it avoids the need for age and sex specific cutoff values because it is corrected for height [6]. A study of 111 Chinese men found that WHtR (.87, p<.001) was better correlated with VAT compared to WC (.82, p<.001), WHR (.65, p<.001), or BMI (.72, p<.001) [67]. In addition, an eight year longitudinal study of 11,000 subjects revealed that WHtR is a better predictor of cardiovascular disease, stroke, or death than

BMI [58]. Westphal et al also observed that WHtR is a good predictor of different metabolic risk indicators (uric acid, TRG, cholesterol, HDL-C, C-reactive protein (CRP), systolic BP, and insulin resistance (HOMA-IR) in 28-84-year-old adults [5].

Physical Activity and Cardiometabolic Risk Independent of Body Fatness

Regular PA of at least moderate intensity has been shown to improve MetS and reduce CMR in general population samples [16, 21, 28, 63]. However, the results of studies that have explored the extent to which PA is associated with reduced CMR independent of body fatness have been conflicting.

In a cross-sectional study of children (9 years, n = 273) and adolescents (15 years, n = 256), PA was not significantly correlated with a summary CMR score, computed as the mean of the standardized outcome scores of fasting insulin, glucose, TRG, total cholesterol, HDL-C, and BP, when adjusted for adiposity [56]. Another study from the Quebec Adipose and Lifestyle Investigation in Youth (QUALITY) cohort which included 630 white children (8-10 years old) revealed that total PA (by accelerometer (counts/min)) is not related to measures of insulin resistance, fasting insulin, or Matsuda index (index of insulin sensitivity based on oral glucose tolerance test) after adjustment for body fatness measured by DXA [23].

In contrast, a meta-analysis of 14 studies that looked at the independent and combined associations between objectively measured time in moderate- to vigorous-intensity PA (MVPA) and sedentary time with CMR risk factors in children (aged 4-18 years) revealed that MVPA is inversely associated with TRG (β-coefficient = -.017, *95% CI* -.025 to -.009) and fasting insulin (β-coefficient = -.028, *95% CI* -.038 to -.017) even after adjustment for WC [16]. Furthermore, a cross sectional study of 192 adolescents (14-16 years old) observed that cardiorespiratory fitness is independently associated with CMR score even after adjusting for WC (β=-0.078, $p<.001$) [7].

While the earlier studies adjusted their results by body fatness measured by DXA and skinfold thickness, the later adjusted their results using WC as a measure of body fatness. This difference in measures used to estimate body fatness across studies provides a plausible explanation for these inconsistent findings. This suggests that the use of different body fatness measures could significantly affect the independent relationship of PA and CMR.

Summary

A large number of studies have explored the relationship between obesity and CMR although most of these correlational studies have relied on BMI to differentiate between obese and normal weight individuals and studies among college-aged adults, especially females, have been scarce. Moreover, differences in methods, especially the lack of uniformity in the anthropometric measure used to estimate body fatness, limit our ability to accurately quantify the public health impact of obesity. Future research is needed to identify the best measure of obesity in different population subgroups and to understand the relationship of these anthropometric measures to CMR, especially in the emerging adult population known to be at increasing risk for obesity. In addition, it is imperative to determine how the adjustment for different body composition measures can influence the observed association between PA and CMR. Determining which anthropometric measure (BMI, WC, or WHtR) is the best predictor of body fatness and CMR factors, and determining their possible effect on the relationship of PA and CMR among college aged- females is a step towards this goal.

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CHAPTER 3

THE UTILITY OF ALTERNATIVE BODY COMPOSITION MEASURES TO ASSESS BODY FATNESS AND CARDIOMETABOLIC RISK IN FEMALE COLLEGE STUDENTS [1]

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Abstract

OBJECTIVE: This study sought to determine which anthropometric measure (body mass index (BMI), waist circumference (WC), WC-to-height ratio (WHtR), or a body shape index (ABSI)) best predicts body fatness and cardiometabolic risk (CMR) and how the choice of body fatness measure affects the observed association between physical activity (PA) and overall CMR in young adult females. DESIGN AND METHODS: Anthropometric measures, body composition via dual energy X-ray absorptiometry (DXA) scan (GE iLunar), PA via accelerometers (NL-1000), and CMR profile were collected in 334 women enrolled at the University of Georgia, Athens. RESULTS: WHtR best predicted both central (r=.84) and total body fat (R^2=.80). Body fat measures were weakly to moderately correlated with indicators of CMR (r of .01 to .51). PA's association with CMR score ranged from standardized beta coefficient (β) of -.44 to β of -.78 when adjusted for different measures of body composition. CONCLUSION: The anthropometric measures WHtR, WC, and BMI can serve as surrogate measures for DXA measured body fatness in college-aged females. There was no single body fat measure that best predicted all indicators of CMR. However, when seeking to quantify the association between PA and CMR score independent of adiposity, the choice of adiposity measure affects the strength of the observed association.

Introduction

Current studies indicate that 7-12% of college students meet the criteria of metabolic syndrome (MetS) and 30-40% exhibit at least one indicator of this condition [8, 17, 29]. In addition, obese college students have been shown to have three times the risk of developing at least one cardiometabolic risk (CMR) indicator [12]. As such, body fatness seems to be a major contributor to CMR. Currently, dual energy X-ray absorptiometry (DXA) is the most accurate method for estimating body composition but this measure is expensive and impractical for screening large populations and also has limited use in clinical practice.

A number of cost-effective anthropometric measures like body mass index (BMI) and waist circumference (WC) are widely used proxy measures of body fatness. These measures have been highly correlated with body fatness in both children [5] and adults [6, 15]. In addition, these anthropometric measures have been shown to correlate with CMR. Westphal et al indicated that WC and WC to height ratio (WHtR) are better predictors of different metabolic risk indicators (uric acid, triglyceride (TRG), total cholesterol, high density lipoprotein cholesterol (HDL-C), C-reactive protein (CRP), systolic blood pressure (SBP), and insulin resistance (HOMA-IR)) in 28-84-year-old adults [4] compared to BMI and total body fat measured by air displacement plethysmography. Furthermore, WC has been shown to be more strongly correlated with CMR than BMI among adults, presumably because WC is a better indicator of intra-abdominal fatness which is highly associated with adverse metabolic profiles [6, 15, 24]. Thus, anthropometric measures based on WC, such as WHtR [4] and A Body Shape Index (ABSI), have been recently proposed as better indicators of health risk and have been shown to be strongly associated with mortality risk [18]. However, few studies have directly compared the utility of these anthropometric indices in predicting CMR in college-aged adults.

Regular physical activity (PA) of at least moderate intensity has been shown to improve MetS and reduce CMR in general population samples [11]. However, the results of studies that explore the extent to which PA is associated with reduced CMR independent of body fatness have been conflicting. Earlier studies by Hunter and colleagues have shown that self-reported PA was not related to cardiovascular disease risk after adjustment for intra-abdominal body fat via computed tomography scan [13, 14]. In a more recent cross-sectional study of children (mean age of 9 years, n = 273) and adolescents (mean age of 15 years, n = 256), minutes of moderate to vigorous PA (MVPA) was not significantly correlated with a summary CMR score, computed as the mean of the standardized values of fasting insulin, glucose, TRG, HDL-C/total cholesterol, systolic blood pressure (SBP) and diastolic blood pressure (DBP), after adjustment for adiposity measured by skinfold thicknesses [21]. In contrast, a meta-analysis of 14 studies that looked at the independent and combined associations between objectively measured MVPA and sedentary time with CMR factors in children (age 4-18 years) revealed that MVPA is inversely associated with TRG and fasting insulin even after adjustment for WC [10]. This is in agreement with the results from the Nurses' Health Study cohort where the authors reported PA to be associated with increased coronary heart disease risk independent of body fatness measured via WC, WHR, or BMI. While the earlier studies adjusted their results by CT-scan and skinfold thickness measures of fatness, the later adjusted their results using more common anthropometric measures as surrogate indicators of body fatness. These differences in body fatness measures across studies provide a plausible explanation for the inconsistent findings reported in the literature regarding PA and CMR factors.

This study aimed to compare the ability of several commonly used anthropometric measures (BMI, WC, WHtR, and ABSI) to predict DXA estimates of total and central body fat

and to examine the association of each measure with indicators of CMR, such as plasma levels of TRG, HDL-C, low density lipoprotein (LDL-C), HOMA-IR, and c-reactive protein (CRP), in college-aged females. Furthermore, we sought to examine the extent to which the choice of body composition measure may affect observed associations in studies seeking to quantify the independent contribution of PA and body composition to cardiometabolic disease risk.

Materials and Methods

Study Design and Subjects

Anthropometric measures, PA, and CMR factors data were combined from the Preventing Obesity by Wellness Education and Responsibility (POWER Dawgs) Study and the Sprint Interval and Nutrition (SPIN Dawgs) Study. Full-time, female, freshmen college students (n=310) aged 18-20 years old enrolled at the University of Georgia, Athens (UGA) in 2012-2013 were recruited in the POWER Dawgs Study while overweight (BMI≥25), female students (n=94) aged 18-24 years enrolled full-time at UGA in 2014-2015 were recruited for the SPIN Dawgs Study. Potential subjects for both studies were excluded if they were varsity athletes, pregnant or planning to become pregnant, or if they had given birth in the previous 12 months. In addition, participants that were diagnosed with any neuromuscular, musculoskeletal, cardiovascular, or cardiopulmonary disorder that is exacerbated by moderate to vigorous exercise or had any health condition that precluded moderate to vigorous exercise were also excluded in the SPIN Dawgs Study. Participants were identified and recruited using the listservs from the Office of the Registrar at UGA. The studies were approved by the University of Georgia Institutional Review Board and all subjects were provided written informed consent prior to participation in the study.

Protocol

Baseline study protocols were very similar for both studies. After eligibility was determined, participants were scheduled for two visits to the measurement laboratory eight days apart. Informed consent and study questionnaires were completed at the initial visit. Blood samples were taken by trained personnel at the University of Georgia Health Center. The participants were also given an accelerometer (New Lifestyle (NL)-1000) that they wore for the next 7 days during all waking hours except when bathing or engaging in any water activities. All anthropometric measurements and blood pressure assessments were completed on the second visit.

Outcome Measures

All baseline procedures and devices used to measure the primary outcomes were similar for both the POWER Dawg and SPIN Dawg studies except for blood pressure measurement (described below).

Anthropometric Measures and Body Composition

Body weight was measured with a calibrated electronic scale (Tanita, Model WB100). Standing height was measured to the nearest 0.1 cm using a digital stadiometer (SECA 424) while the participant was barefoot. WC was measured thrice at two different locations: the narrowest area of the waist and at the level of the umbilicus. The average of the three measurements was used as the measure of WC. BMI (kg/m^2) was calculated by dividing weight (kg) by the square of the height (m). WHtR was calculated as the quotient of WC (cm) and height (cm). ABSI was obtained by dividing WC (m) by the product of BMI raised to 2/3 and the square root of height [18]. Whole body and regional soft tissue composition were measured by DXA (GE iLunar). The android fat percentage was used as a measure of central adiposity.

Physical Activity

PA was objectively assessed over a continuous 7-day period using New Lifestyle (NL-1000) Accelerometers. The participants were asked to wear the accelerometer on their non-dominant hip during all waking hours except when bathing or engaging in water activities. During this time, participants were asked to continue to perform their usual daily activities. Participants having less than 4 measurement days with at least 10 hours/day of valid wear time were excluded from the analysis. The average minutes spent in moderate to vigorous PA per day (MVPA/day) and average steps per day (steps/day) were used as measures of free-living PA in this study.

Clinical Measures

All blood samples were collected after an overnight fast via venipuncture in the University Health Center and all biochemical analyses were conducted using a nationally certified lab (Quest Diagnostics). The standard lipid profile (total cholesterol, HDL-C, LDL-C, and TRG) as well as glucose were measured from blood samples using spectroscopy. Plasma insulin levels were measured using immunoassay, and high-sensitivity CRP was analyzed using laser nephelometry.

In the POWER Dawgs study, blood pressure was measured twice in the left arm with measurements done 5 minutes apart while the participant was in a seated position. If there was a difference of more than 5 mmHg for either the systolic or the diastolic value, another BP reading was done. If two readings were taken, average values were used in this analysis. If three readings were obtained, the two values within 5 mmHg were averaged and used. In the SPIN Dawgs study, participants were first asked to rest in a supine position for 10 minutes. Then blood pressure was taken once in the left arm while the participant was in a seated position.

Statistical Analyses

Descriptive statistics were used to characterize the sample of female college students including means and standard deviations for continuous variables and percentages for categorical variables. The distribution of each variable was inspected for normality and non-normal variables were log transformed to approximate a normal distribution. HOMA-IR and minutes of MVPA remained highly skewed even after log transformation. For these variables, a 2-step transformation approach was completed where [28] the variables were converted to percentile ranks to form uniformly distributed probabilities and then an inverse-normal transformation was applied using the mean and standard deviation of the original values to create variables with normally distributed z-scores. Regression curve estimation analyses were used to quantify and compare associations between different anthropometric measures with both total (%Total Fat) and central (%Central Fat) body fat measured by DXA allowing a comparison of linear and non-linear models of these relationships between the two variables. In addition, area under the receiver operating characteristic (AUROC) analysis was employed to explore the ability of these alternative anthropometric measures to identify females with high body fat percentage measured by the DXA scan (body fat > 35%).

Relationships between body composition measures and CMR factors were also assessed using regression curve estimation analyses and partial Pearson correlation adjusted for age and oral contraceptive use. An overall CMR score was calculated using the sum of standardized z-scores for TRG, HDL-C, SBP, and the negative inverse of HDL-C (to account for beneficial effects of higher HDL-C level). Linear regression analyses were then used to examine whether the use of different body fatness measures substantially affects the magnitude of association between PA and CMR independent of body fatness. All statistical analysis were conducted using

IBM SPSS Statistics for Windows (SPSS 21.0, Chicago, IL) with statistical significance set at an alpha level of .05.

Results

Participants

Participants missing a CMR factor, anthropometric measure, DXA scan, or PA measure, were excluded from this analysis. Of the 403 female college students from both studies (n=310 from POWER Dawgs and n=94 from SPIN Dawgs), 334 (n=276 from POWER Dawgs and n=58 from SPIN Dawgs) females had complete data. Table 1 summarizes the demographic and cardiometabolic profiles of the sample participants. The mean age of the participants was 18.6±1.0 years. The sample consisted mostly of Caucasians and African-Americans, at 71% (237/334) and 13% (42/334) respectively. Overall, 66% (222/334) of the participants had BMI values in the normal weight category, 22% (72/334) in the overweight category, and 12% (40/334) in the obese category. CMR profiles were predominantly within normal ranges across risk factors. The participants accumulated an average of 10,113±3704 steps/day and 43.4 (*Confidence Interval (CI)* 31.2-56.7) minutes of MVPA/day.

Predicting Body Fatness through Anthropometry

Table 2 summarizes the relationship of different anthropometric measures to both total and central percent body fat measured by DXA. The analyses revealed, as expected, positive moderate correlations between the anthropometric measures and DXA-measured body fat and, overall, stronger associations with central fat better than with total body fat. WHtR was the best predictor of both %Total Fat (r=.80, p<.001) and %Central Fat (r=.84, p<.001) although other anthropometric measures such as WC and BMI also showed similar predictive power. The ABSI measure had negligible associations with both DXA measures of body fatness, which is perhaps

not surprising considering that it has been shown to have little correlation with BMI [18]. Moreover, the differences between linear and non-linear models for these anthropometric measures and DXA measured body fat were not robust enough to warrant deviation from linear modelling.

To determine how well these anthropometric measures differentiate individuals that are overweight or obese based on DXA measures (%Fat>35%), the AUROC analysis was employed (Table 3). BMI and WHtR had a good ability (AUROC=.89-.90, $p<.001$) to discriminate individuals that were overweight/obese as identified by DXA. Although not as good as BMI and WHtR, WC was also effective in discriminating individuals that have a high fat percentage. The WC-U provided a good measure to identify those with high total and central fat percentage (AUROC=.87 and .86 respectively) although the WC-N was slightly more accurate (AUROC=.88 for %Fat Total and .87 for %Fat Central). Similar to the results from table 2, ABSI performed poorly in discriminating individuals with high total or central fat.

Measures of Body Fatness and Cardiometabolic Risk Factors

Examination of the relationship between different anthropometric and DXA measures of body fatness (BMI, WC, WHtR, %Total Fat, %Central Fat, and ABSI) with important CMR factors revealed varying levels of weak to moderate associations (Table 4). For plasma TRG, %Fat Central had the strongest correlation among the alternative measures ($r=.23$, $p<.001$) although %Total Fat was also similarly correlated. WC-U showed the highest correlation among the anthropometric measures. On the other hand, WC-N showed the strongest association with HDL-C ($r=-.26$, $p<.001$). Slightly weaker correlations were also seen with other measures of body fatness except for ABSI. Correlations between the different measures of body fatness and LDL-C revealed negligible to weak associations, with %Central Fat having the strongest

correlation (r=.15, p<.01). BMI provided the strongest correlation with SBP (r=.51, p<.001) and other anthropometric measures also showed moderately strong correlations (r of .37-.50, p<.001). Surprisingly, both DXA measures of body fatness had weaker correlations compared to the anthropometric measures. Across these analyses, HOMA-IR had the strongest associations (r of .44-.50, p<.001) with all the different body fat measures, with the correlation highest for BMI and WC-N. ABSI was not strongly associated with any of the CMR factors.. Quadratic and cubic models between these measures of body fatness and CMR factors were examined (Supplemental Table 1); however, these models offered only small improvements in the strength of associations between variables of interest (.01-.05 increase in r value).

A logistic regression analysis (Table 5) was utilized to look at the relationship of the different measures of body fatness and CRP. Because it was positively skewed and unable to be normalized by transformation, CRP was converted into a binomial categorical variable to indicate high CRP values (CRP>3 mg/L) [27]. Results indicated that %Total Fat was the strongest predictor of increased CRP levels where a standard deviation increase in %Total Fat was associated with a 3.50 (*95% CI* 2.10-5.82) times increased risk of having high CRP. Associations for other measures of body fatness were only marginally weaker (ORs ranged from 2.08-2.76). Similar to the results above, ABSI showed the weakest relationship with CRP. In addition, a similar analysis was conducted using high CMR level as the outcome variable. CMR was transformed into a categorical variable with the 85^{th} percentile value (2.45) used as the cut point for high CMR level. %Central Fat was the strongest predictor of high CMR level where a standard deviation increase in %Central Fat was associated with a 7.99 (*95% CI* 4.35-14.68) times increase in risk of having high CMR. Anthropometric measures of body fatness showed

weaker associations with ORs ranging from 4.04-4.63 except for ABSI which showed a relatively poor predictive capacity (OR=1.38, *95% CI* 1.00-1.91).

Physical Activity and Cardiometabolic Risk

Table 6 summarizes the relationship between both average steps/day and minutes of MVPA with a summary CMR score unadjusted (Model A) and following adjustment for alternative measures of body fatness (Models B-H). Associations between PA and CMR score (both adjusted and unadjusted for fatness) were very similar across the different PA measures. PA alone was a significant predictor of CMR score (Model A) (β of -0.79 for steps/day and -0.78 for MVPA/day). As expected, the strength of this association was generally attenuated upon adjustment for body fatness. However, the degree to which the PA coefficients were reduced varied depending on the type of body fat measure used in the model. The smallest reduction in PA coefficients was seen when ABSI was used as a measure of body fatness with a standardized beta coefficient of -0.78 (*95% CI* -1.04 to -0.53) and -0.77 (*95% CI* -1.04 to -0.51) for steps/day and MVPA/day respectively. The largest attenuation was seen upon adjustment for %Total Fat with standardized beta coefficient of -0.44 (*95% CI* -0.69 to -0.19) and -0.43 (*95% CI* -0.69 to -0.18) for steps/day and MVPA/day respectively.

The multiple coefficient of determination also varied across models including different measures of body fatness (multiple R^2 of .24 to .43). Model E (PA+WC-N) produced the highest coefficient of determination value (.43, $p<.001$ for steps/day and .41, $p<.001$ for MVPA/day) among the different models. To expand on this, WC-N and steps were divided into tertiles and then analyzed using univariate ANOVA (Figure 1). There was a significant steps*WC-N interaction ($F(4, 320)=2.87$, $p=.04$). For the 1st and 2nd tertile of WC-N, there were no significant differences in CMR of participants across different tertiles of steps. However, among those in the

3rd tertile of WC-N, mean CMR was significantly different across tertiles of steps/day. Specifically, mean CMR among those in the 1st tertile of steps was significantly higher than for those in the 2nd and 3rd tertiles. This result suggests that in this population of relatively healthy young adults, steps/day significantly improves CMR profiles only among those individuals with higher WC-N.

Discussion

In a cross-sectional analysis of 334 college-aged students, we explored the association of different anthropometric measures of body fatness to total and central body fat and their ability to predict CMR to determine their usefulness in identifying college-aged females at high CMR. In addition, we assessed the effect of using different measures of body fatness when seeking to quantify the independent relationship of PA to CMR.

In predicting DXA measured body fatness, WHtR was the best predictor of both total and central body fat percentage. This is similar to the results from a study [4] where different anthropometric measures of 335 adults (mean age of 53±13.9 years) were correlated with body fat percentage measured by air displacement plethysmography whereas WHtR was the best predictor of body fat percentage (r=.73, p<.001), followed by WC (r=.70, p<.001), and then by BMI (r=.69, p<.001). One key strength of the present analysis is that central body fat was quantified, which has been highly correlated with CMR [19], which allowed us to evaluate the relationship of anthropometric measures to central as well as total body fatness. Notably, WC-N, WC-U, and WHtR were observed to have stronger associations with %Central Fat compared to %Total Fat. Surprisingly, we saw similar results with BMI, which is a surrogate measure of overall body fatness. Although several studies have reported that BMI is inaccurate at discriminating individuals with high body fat percentage [2, 16, 22], the present data showed that

BMI and both WC measurements have similar associations with %Central Fat. In addition, the AUROC analysis revealed that WHtR, BMI, WC-N, and WC-U have similar abilities for discriminating individuals with elevated levels of both total and central body fat. These results align with the results from a previous cross sectional study [1] where WC and BMI performed similarly in terms of identifying individuals with high levels of central fat. The authors concluded that there is not enough evidence to discontinue the use of BMI in the clinical setting for identifying obese individuals that are at high risk for cardiometabolic disease. The mixed ability of these alternative measures of body fatness to predict different CMR factors in the current study also supports this notion.

The ultimate purpose of determining the best surrogate measure of body fatness is to inform the selection of practical and cost-effective methods for identifying individuals that are at high risk for cardiometabolic disease in different population subgroups. Analysis of the association of alternative fatness measures, including both DXA measures of body fat, with different CMR factors revealed that there is no one measure that most strongly correlated with all risk factors. Overall, the associations of the body fat measures used in the study with different lipid measures were negligible to weak at best. These correlations are hardly unexpected considering the results from an earlier study showing similarly weak correlations [23]. Although a number of large studies have reported that body fatness is strongly associated with adverse lipid profiles, most of these studies have been conducted in older population [9, 26]. A study that evaluated the relationship of body fatness with lipid profiles in adolescents (age 14-19 years old) reported weaker associations between lipid indices and BMI and %Total Fat by bioelectrical impedance among females [7]. This suggests that, compared to older adults, younger individuals may be better able to regulate their lipid profile despite high levels of adiposity.

Another interesting finding from this analysis is that linear models do not adequately describe all the associations between body fatness measures and CMR. A quadratic model was found to provide a slightly better fit of the relationships between HOMA-IR and all of the alternative measures of body fatness. Moreover, a quadratic model also best fit the association of %Central Fat with TRG, HDL-C, LDL-C and SBP and %Total Fat with TRG and SBP. These quadratic relationships suggest varying associations between body fatness and CMR factors across different levels. For example, in individuals with low %Central Fat (<35%), body fatness and SBP shows no correlation but in individuals with high %Central Fat (≥35%), the relationship becomes linear (Supplemental Figure 2). These differences in the functional relationship between alternative body composition and cardiometabolic indicators could, if not accounted for, limit the ability of these measures to accurately predict select CMR outcomes.

One unexpected finding from this study was that %Central Fat, which is the most accurate measure of central body fatness in this study, was only better at predicting two of five CMR factors (TRG and LDL-C) when compared to the other surrogate measures of body fatness. This may be due to the fact that %Central Fat from DXA, although highly correlated with visceral adipose tissue (VAT) measures from MRI or CT scan [3, 20, 30], could not directly distinguish visceral fat from subcutaneous fat. Essentially, the DXA measured central fatness is a measure of the overall abdominal adiposity and not necessarily of VAT. In contrast, previous studies have shown that WC-N has a stronger association with VAT measured by MRI compared to other WC measurement sites [24, 25]. This may partially explain why WC-N had stronger correlations with HDL-C, HOMA-IR and SBP than WC-U despite having similar correlations with %Central Fat by DXA.

This study examined the effect of using different measures of body fatness on the strength of relationship between CMR and PA. Our results indicate that using different measures of body fatness to quantify the body fat independent effect of PA on CMR minimally affected the strength of the relationship between the two variables. PA remained a significant predictor regardless of the measure of PA or body fatness used in the model. Nevertheless, this analysis indicated that body fatness plays a critical role in terms of modeling the association between PA and CMR. As different fatness models correlated differently with our summary measure of CMR, the coefficient of determination of each model and the regression coefficient of PA varied depending on the measure of body fatness that was used. Models utilizing DXA measured body fatness resulted in weaker relationships between PA and overall CMR due to stronger correlations between these measures of body fatness and overall CMR. Despite this, the overall fit of the model was lower compared to models using other anthropometric measures except for ABSI. This could be explained by non-linear relationships observed in DXA measured body fatness and ABSI with different CMR factors. The non-linear relationship between these variables could have caused the lower association between DXA measured body fat and overall CMR score in this sample. To test this hypothesis, the quadratic term of the particular body fatness measure was used in place of the linear terms in models B, C, and H (Supplemental Table 2). The coefficient of determination remained the same for both models with DXA measured body fat and ABSI although standardized beta coefficients for both the DXA measures improved slightly with steps/day. The improvement in the coefficient of determination indicates that the quadratic relationship accounts for some but not all of the reason why we see lower associations in CMR when using the DXA measures. Further research in this population is needed to explore other possible factors that might cause this observation.

Although our data is of interest, especially for the emerging adult female population known to be increasing risk for obesity, our study is not without recognized limitations. One limitation of this study is that it included only young, college-aged females who were mostly Caucasians and attending a major research institution in the southeast. Therefore, conclusions made from this study may not generalize to other college-aged populations that are more racially diverse. In addition, the sample of participants primarily consisted of healthy individuals with normal CMR factor levels. Further, the accelerometer used in this study uses different cutoff points to determine MVPA that are different from the validated accelerometer cutoff point counts being used by most research grade accelerometers.

Conclusion

Overall, the present study suggests that various anthropometric measures of body fatness such as WHtR, WC, and BMI could serve as valid surrogate indicators of both central and total body fat in college-aged females. No single body fat measure was most strongly associated with all the CMR factors measured for this study. However, WC-N was most strongly associated with overall CMR score among the anthropometric measures. Lastly, the choice of body fatness measure was observed to have only a modest impact on the strength of relationship between PA and CMR in this population.

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Table 1. Demographic and cardiometabolic profile of college-aged females (n = 334).

	Mean±SD or Median(25^{th}, 75^{th})
Age	18.7±1.1
Weight (kg)	65.9±13.8
Height (cm)	164.6±6.4
Body Fat Measures	
%Total Fat	35.1±6.9
%Central Fat	38.4±11.7
BMI	23.1(20.9, 26.9)
Waist circumference	
Normal waist circumference (cm)	72.3(67.2, 79.9)
Umbilical waist circumference (cm)	81.2(74.4, 89.5)
Waist-to-Height Ratio	0.44(0.41, 0.49)
Cardiometabolic Risk Factors	
Blood Pressure	
Systolic (mmHg)	115.2±13.4
Diastolic (mmHg)	71.3±10.1
Lipid Profile	
Total Cholesterol (mg/dL)	162.0(146.7, 184.3)
LDL-C (mg/dL)	86.0(71.0, 103.0)
HDL-C (mg/dL)	60.3±14.5
Triglycerides (mg/dL)	75.0(58.0, 102.0)
Glucose (mg/dL)	85.0(81.0, 89.0)
Insulin (μIU/mL)	3.0(1.0, 6.0)
HOMA-IR	0.64(0.2, 1.3)
CRP (mg/L)	0.85(0.2, 2.3)
Physical Activity	
Steps/day	10113±3704
Minutes of MVPA/day	43.4(31.2, 56.7)

%Total and %Central fat as measured by dual energy X-ray absorptiometry. LDL-C: low density lipoprotein cholesterol. HDL-C: high density lipoprotein cholesterol. HOMA-IR: homeostatic model assessment of insulin resistance. CRP: C-reactive protein. MVPA: moderate to vigorous intensity physical activity.
All values expressed by mean±SD for normally distributed variables and median (25th, 75th percentile) for skewed variables.

Table 2. R of curve estimation regression between DXA and anthropometric measures of body fat.

	%Total Fat	%Central Fat
BMI		
Linear	.79	.81
Quadratic	.79	.81
Cubic	.79	.81
WC-N		
Linear	.77	.81
Quadratic	.77	.81
Cubic	.77	.81
WC-U		
Linear	.77	.81
Quadratic	.77	.81
Cubic	.77	.81
WHtR		
Linear	.80	.84
Quadratic	.81	.84
Cubic	.81	.84
ABSI		
Linear	.17	.24
Quadratic	.22	.26
Cubic	.22	.26

BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index.
All relationships are significant at $p<.001$ except for linear model of %Fat Total and ABSI ($p<.01$).

Table 3. Area under the receiver operating characteristic curve analysis of different anthropometric measures for recognizing DXA identified overweight/obese individuals.

	Area	SE
BMI		
Total	.90	.02
Central	.89	.02
WC-N		
Total	.88	.02
Central	.87	.02
WC-U		
Total	.87	.02
Central	.86	.02
WHtR		
Total	.89	.02
Central	.89	.02
ABSI		
Total	.55	.03
Central	.55	.03

BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index.
All relationships are significant at $p<.001$ except for ABSI.

Table 4. Partial correlation coefficients[†] between different measures of body fatness and cardiometabolic risk factors.

	TRG	**HDL-C**	**LDL-C**	**HOMA-IR**	**SBP**
BMI	.09	-.23***	.11	.50***	.51***
WC-N	.14*	-.26***	.11*	.50***	.50***
WC-U	.18**	-.24***	.12*	.47***	.45***
WHtR	.15**	-.24***	.13*	.49***	.46***
% Total Fat	.22***	-.21**	.12*	.44***	.37***
%Central Fat	.23***	-.24***	.15**	.44***	.38***
ABSI	.16**	-.07	.06	.06	.01

BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index. TRG: triglycerides. HDL-C: high density lipoprotein cholesterol. LDL-C: low density lipoprotein cholesterol. HOMA-IR: homeostatic model assessment of insulin resistance. SBP: systolic blood pressure.

%Total and % Central fat as measured by dual energy X-ray absorptiometry.

[†]Adjusted for oral contraceptive use and age.

Significant at *p<.05**p<.01***p<.001.

Table 5. Logistic regression of CRP and CMR with different body fat measures.

	High CRP‡		High CMR†	
	OR*	**95% CI**	**OR***	**95% CI**
BMI	2.08	1.51-2.86	4.04	2.68-6.10
WC-N	2.59	1.83-3.65	4.63	2.98-7.18
WC-U	2.60	1.83-3.70	4.51	2.87-7.07
WHtR	2.33	1.67-2.25	4.06	2.69-6.13
%Total Fat	3.50	2.10-5.82	7.50	3.99-14.10
%Central Fat	2.76	1.80-4.24	7.99	4.35-14.68
ABSI	1.67	1.21-2.32	1.38	1.00-1.91

CI: confidence interval. BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index. CRP: C-reactive protein. CMR: cardiometabolic risk score.

Adjusted for oral contraceptive use and age.

*For 1 standard deviation increase in body fatness measure.

‡From categorical transformation with CRP>3 mg/L indicating high levels.

† From categorical transformation with CMR>2.45 indicating high levels.

Table 6. Standardized regression coefficients (β) and standardized coefficient of determination (R^2) examining the association of physical activity and cardiometabolic risk using different surrogate measure of body fatness.

	Steps/day			Mins/day		
	R^2	β*	*95% CI*	R^2	β*	*95% CI*
Model A	.23			.22		
PA		-0.79	(-1.05, -0.53)		-0.78	(-1.05, -0.52)
Model B	.37			.37		
PA		-0.44	(-0.69, -0.19)		-0.43	(-0.69, -0.18)
%Total Fat		1.61	(1.23, 1.98)		1.62	(1.25, 2.00)
Model C	.38			.38		
PA		-0.46	(-0.71, -0.22)		-0.45	(-0.70, -0.20)
%Central Fat		1.42	(1.12, 1.72)		1.42	(1.11, 1.73)
Model D	.41			.40		
PA		-0.56	(-0.79, -0.33)		-0.49	(-0.73, -0.24)
BMI		1.20	(0.96, 1.44)		1.19	(0.95, 1.43)
Model E	.43			.41		
PA		-0.54	(-0.76, -0.31)		-0.44	(-0.68, -0.20)
WC-N		1.30	(1.06, 1.54)		1.29	(1.04, 1.54)
Model F	.41			.39		
PA		-0.55	(-0.78, -0.31)		-0.45	(-0.70, -0.21)
WC-U		1.21	(0.97, 1.45)		1.20	(0.95, 1.45)
Model G	.41			.40		
PA		-0.58	(-0.81, -0.35)		-0.50	(-0.74, -0.26)
WHtR		1.24	(1.00, 1.48)		1.23	(0.98, 1.47)
Model H	.24			.23		
PA		-0.78	(-1.04, -0.53)		-0.77	(-1.04, -0.51)
ABSI		0.29	(0.02, 0.57)		0.27	(-0.01, 0.55)

CI: confidence interval. BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index. Cardiometabolic risk score calculated as the sum of the z-scores of triglycerides, inverse of high density lipoprotein cholesterol, homeostatic model assessment of insulin resistance, and systolic blood pressure.

Physical activity as measured by NL-1000 accelerometers.

%Total and % Central fat as measured by dual energy X-ray absorptiometry.

Adjusted for age and oral contraceptive use.

*Standardized beta coefficients.

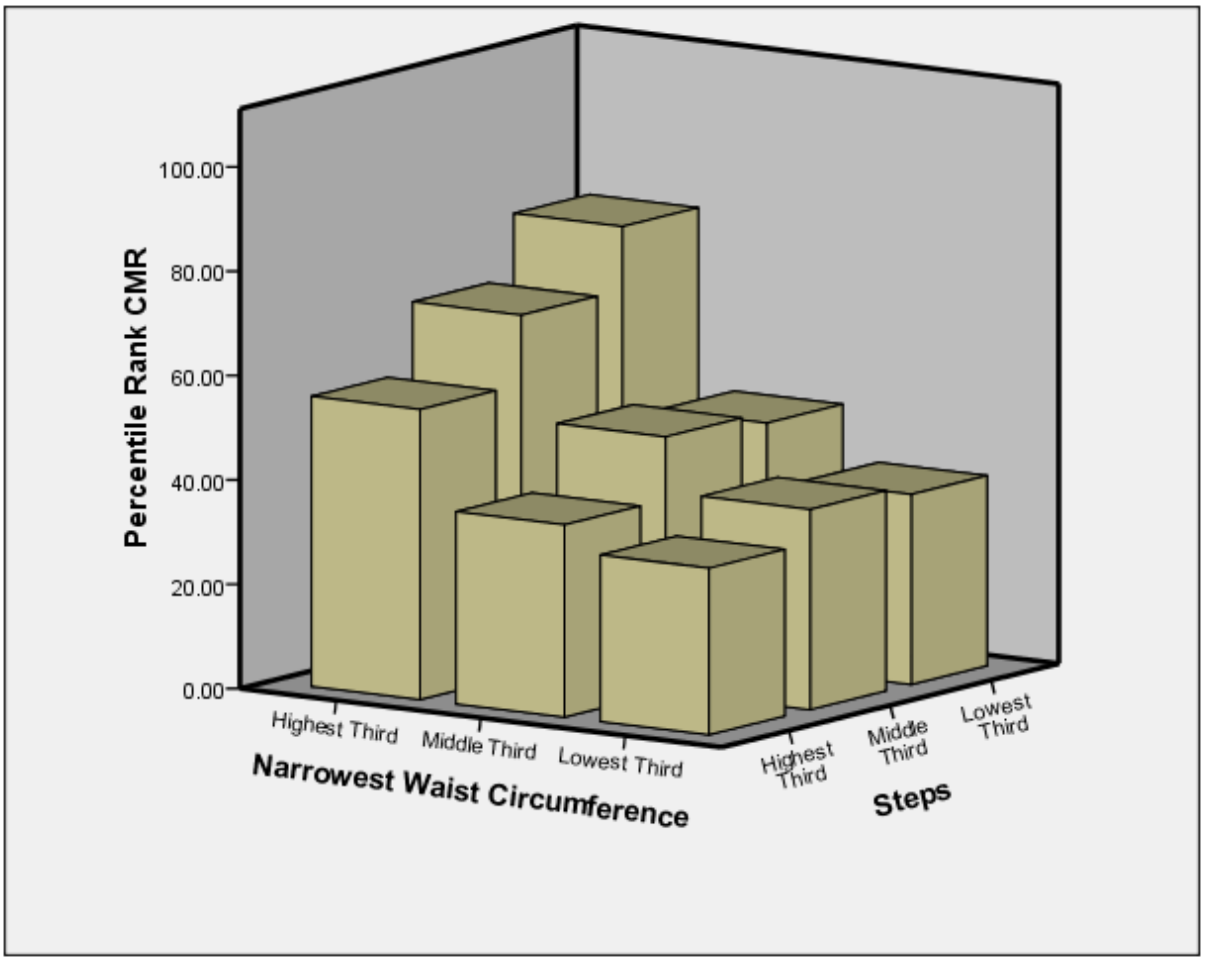

Figure 1. Mean percentile cardiometabolic risk (CMR) score across tertiles of narrowest waist circumference and steps.

CHAPTER 4

DISCUSSION

The current epidemic of obesity, not only in the United States but worldwide, has accelerated research on obesity and its impact on public health, especially in terms of cardiometabolic risk (CMR).. Several anthropometric measures have been developed to serve as surrogate measures of body fatness and predictors of CMR. However, the exact relationship of these measures to different CMR factors in college females has not been previously explored [5-7, 17, 19]. Furthermore, the lack of uniformity in the methods used to estimate body fatness and predict CMR potentially explains the contradicting results from studies that have evaluated the effect of physical activity (PA) on CMR independent of body fatness [13, 15, 23]. Therefore, identifying a standard anthropometric measure that strongly predicts body fatness and CMR is of both research and clinical interest. These analyses aimed to 1) increase understanding of the relationship between different anthropometric measures and DXA measured body fatness outcomes, 2) explore how various anthropometric measures and DXA outcomes associate with different CMR factors, and 3) how the use of different measures of body fat can affect the observed relationship of PA and CMR. Specifically, WC, BMI, WHtR, ABSI and DXA measures of body fatness were evaluated in their ability to predict different CMR factors, including triglycerides (TRG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), homeostatic model assessment of insulin resistance (HOMA-IR), and systolic blood pressure (SBP), in college-aged women.

Three hundred thirty-four college-aged women enrolled at the University of Georgia, Athens were examined in this study. Anthropometric body measures and DXA scans were recorded and multiple CMR factors measured. Participants were also asked to wear an accelerometer for seven days to quantify average daily steps and minutes of MVPA.

Overall, WHtR was found to be the best anthropometric measure predictor of both total and central body fat. One key strength of this analysis is that we quantified central body fat, which has been highly correlated with CMR [20], which allowed us to evaluate the relationship of anthropometric measures to central as well as total body fatness. WC-N, WC-U, and WHtR were observed to have stronger associations with %Central Fat compared to %Total Fat. Surprisingly, we saw similar results with BMI, which is a surrogate measure of overall body fatness. Additional AUROC analysis revealed that WHtR, BMI, WC-N and WC-U have similar capabilities in discriminating individuals that have increased levels of both total and central body fat. The mixed ability of these anthropometric and DXA measures of body fatness to predict different CMR factors further supports this notion.

A central purpose of this study was to determine the best surrogate measure of body fatness to inform the selection of practical and cost-effective methods for identifying individuals that are at high risk for cardiometabolic disease in different population subgroups. Previous studies [21, 32] have indicated that in the presence of other information on risk factors such as HOMA-IR, hypertension, and HDL-C, anthropometric measures of obesity do not improve prediction of cardiovascular diseases. Although this may be true, it does not diminish the importance of assessing body fatness especially its use as an initial screening tool to identify individuals at risk for developing cardiometabolic diseases. The analysis of the relationship of anthropometric and DXA measures of body fatness with different CMR factors found that no

single measure of body fatness correlated strongly with all risk factors. In addition, the associations of the body fat measures used in this study with lipid measures were weak at best.

It should be noted that this analysis is only valid for identifying individuals that are at higher risk for developing cardiometabolic disease and not the predictive value of body fatness on disease outcomes per se. However, previous studies [29-31] have already shown that the presence of CMR factors increases an individual's risk of developing type 2 diabetes or cardiovascular disease. Furthermore, a study [10] evaluating the prevalence of metabolic syndrome in younger population using the NHANES data suggested that an increase in the number of CMR factors in childhood and adolescents usually "tracks into adulthood". Another study [3] of 999 members of 111 extended Midwestern US families of Northern European origin concluded that adiposity at the waist is a more significant predictor of metabolic syndrome traits in children and adolescents than it is in adults. These evidences augment the practice of using different anthropometric measures to predict CMR of an individual in this population.

The analysis of the current data also revealed that a linear model does not entirely describe the relationship between these body fat measures and CMR factors. A quadratic model was found to be a better fit of the relationships between HOMA-IR and all of the alternative measures of body fatness. Moreover, a quadratic model also best fit the association of %Central Fat with TRG, HDL-C, LDL-C and SBP and %Total Fat with TRG and SBP. These quadratic relationships suggest varying associations between body fatness and CMR factors across different levels. For example, in individuals with low %Central Fat (<35%), body fatness and SBP shows no correlation but in individuals with high %Central Fat (≥35%), the relationship becomes linear (Supplemental Figure 2). These differences in the functional relationship between

alternative body composition and cardiometabolic indicators could, if not accounted for, limit the ability of these measures to accurately predict select CMR outcomes.

Unexpectedly, %Central Fat, which is the most accurate measure of central body fatness in this study, was only better at predicting two of five CMR factors (TRG and LDL-C) when compared to the other surrogate measures of body fatness. This may be due to the fact that %Central Fat from DXA, although highly correlated with visceral adipose tissue (VAT) measures from MRI or CT scan [4, 22, 33], could not directly distinguish VAT from subcutaneous fat. Essentially, DXA measured central fatness is a measure of overall abdominal adiposity and not necessarily of VAT. In contrast, previous studies have shown that WC-N has a stronger association with VAT measured by MRI compared to other WC measurement sites [26, 27]. This may provide an explanation for why WC-N had stronger correlations with HDL-C, HOMA-IR and SBP than WC-U despite WC-N and WC-U having similar correlations with %Central Fat by DXA.

Another unexpected finding in this analysis was how poorly ABSI correlated with DXA measured body fatness and the different CMR factors measured in this study. This is contrary to the results of some [12, 18] but not all studies [8, 14]. The disparity in results may be due to the different demographic characteristics of the participants in this study. In addition, Krakauer [18] developed ABSI using mortality risk as the outcome while CMR was evaluated in the current study. Other studies that have measured the independent relationship of ABSI to other cardiometabolic outcomes like hypertension [8] and new onset diabetes mellitus [14] have also revealed no better associations than BMI or WC.

Another aim of this study was to determine the effect of using different measures of body fatness on the strength of the relationship between CMR and PA. Our results indicated that the

strength of this relationship varies depending on the measure of body fatness used in the analysis; although PA remained a significant predictor of CMR throughout the models. The analysis also indicated that body fatness plays a critical role in terms of modeling PA with CMR. The coefficient of determination of each model varied depending on the measure of body fatness that was included in the model. As different fatness models correlated differently with our summary measure of CMR, the coefficient of determination of each model and the regression coefficient of PA varied depending on the measure of body fatness that was used. Models utilizing DXA measured body fatness and ABSI resulted in weaker relationships between PA and CMR and the overall fit of the model was lower compared to models using other anthropometric measures. This could be explained by the non-linear relationships that DXA measured body fatness and ABSI were observed to have with different CMR factors. The non-linear relationship between these variables could have caused the lower association between DXA measured body fat and overall CMR in this sample.

To test this hypothesis, a quadratic term of the particular body fatness measure was used in models B, C, and H (Supplemental Table 1). The coefficient of determination remained the same for all models. However, the in models using steps/day as a measure of PA, the standardized beta coefficients of PA were slightly improved. The improvements in the standardized beta coefficients indicate that the quadratic relationship partially explains why we see weaker associations between DXA measures and CMR. Further research in this population is needed to explore other possible factors that might cause this observation.

Strengths

1. A novel part of this study was that it considered different models to describe the relationships between different anthropometric measures of body fat and DXA measured

body fatness and the relationship of these body fat measures with different CMR factors. Previous studies that have looked at relationships between these variables have only used linear models, potentially missing non-linear relationships between variables. This approach allowed us to more accurately assess the nature of these relationships in college-aged women, enabling us to make better prediction models that could help identify individuals with high percent fat and, subsequently, high risk for developing cardiovascular disease.

2. This study was also looked at the effect of using different measures of body fatness on the relationship between PA and CMR. Two objective measures of PA were used in this analysis: steps/day and minutes of MVPA/day. Although several studies have looked at the independent effect of PA on CMR, results from these studies have been inconsistent, potentially due to differences in outcomes and/or measures utilized. This study suggests that using different measures of body fatness does not significantly diminish the effect of PA on CMR.
3. The use of DXA to measure both total and central body fat percentage in this population is also a major strength of this study. Although several studies have also evaluated these anthropometric measures of body fatness in terms of their ability to estimate body fatness and predict CMR, studies have usually utilized measures that provide less accurate measurement of body fatness like bioelectrical impedance analysis and skinfold measurement. Furthermore, anthropometric measures were also evaluated in terms of their ability to predict central fatness, the measure that they are developed to estimate. The number of participants included in this analysis along with the accurate measures of body fatness lends support to the validity of the results.

Limitations

1. One limitation of this study is that it was limited to young, sedentary, college-aged students of the University of Georgia, Athens. While this precluded confounding of the study results by these factors, it also limits the generalizability of our results to similar populations.
2. The accelerometer used in this study only measured step counts and total minutes of MVPA in a day. The accelerometer did not provide the counts per epoch data which allow estimates of MVPA in bouts of more than 10 minutes. Caution is needed when comparing these results to other studies using bouts of MVPA as the measure of PA.

Conclusion

Overall, the present study suggests that various anthropometric measures of body fatness such as WHtR, WC, and BMI could serve as surrogate indicators of body fat in college-aged females although WHtR was most strongly associated with both central and total body fat measures. No single body fat measure was the best predictor of all the CMR factors measured for this study. However, WC-N was most strongly associated with overall CMR score. Lastly, the choice of body fatness measure was observed to have only a modest impact on the strength of the relationship between PA and CMR in this population.

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APPENDIX A

Table 1. R of curve estimation regression analysis of different measures of body fatness and cardiometabolic risk factors.

	TRG	HDL-C	LDL-C	HOMA-IR	SBP
BMI					
Linear	.11	.20***	.11*	.56***	.58***
Quadratic	.13	.21**	.11	.57***	.58***
Cubic	.13	.21**	.11	.57***	.58***
WC-N					
Linear	.16**	.21***	.12*	.57***	.59***
Quadratic	.17**	.22***	.12	.59***	.59***
Cubic	.17**	.22***	.12	.59***	.59***
WC-U					
Linear	.18**	.20***	.13*	.54***	.55***
Quadratic	.19**	.20**	.13	.56***	.55***
Cubic	.19**	.20**	.13	.56***	.55***
WHtR					
Linear	.17**	.20***	.13*	.56***	.56***
Quadratic	.18**	.20***	.14*	.57***	.56***
Cubic	.18*	.20***	.14	.58***	.56***
% Total Fat					
Linear	.22***	.18**	.13*	.51***	.48***
Quadratic	.24***	.18**	.13	.54***	.52***
Cubic	.24***	.18*	.13	.55***	.53***
%Central Fat					
Linear	.21***	.21***	.14**	.51***	.47***
Quadratic	.24***	.22***	.15*	.55***	.52***
Cubic	.25***	.22**	.16*	.55***	.52***
ABSI					
Linear	.20***	.05	.08	.15**	.13*
Quadratic	.20**	.09	.09	.19**	.19**
Cubic	.20**	.09	.09	.19**	.19**

BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index. TRG: triglycerides. HDL-C: high density lipoprotein cholesterol. LDL-C: low density lipoprotein cholesterol. HOMA-IR: homeostatic model assessment of insulin resistance. SBP: systolic blood pressure.

%Total and % Central fat as measured by dual energy X-ray absorptiometry.

Significant at *p<.05**p<.01***p<.001.

APPENDIX B

Table 2. Standardized regression coefficients (β) and standardized coefficient of determination (R^2) examining the association of physical activity and cardiometabolic risk using different surrogate measure of body fatness with quadratic term.

	Steps/day			Mins/day		
	R^2	**β***	***95% CI***	***R^2***	**β***	***95% CI***
Model A	.36			.36		
PA		-0.47	(-0.72, -0.22)		-0.42	(-0.68, -0.16)
%Total Fat^2		1.04	(0.79, 1.29)		1.04	(0.79, 1.30)
Model B	.38			.37		
PA		-0.51	(-0.75, -0.27)		-0.47	(-0.72, -0.22)
%Central Fat^2		1.02	(0.79, 1.25)		1.02	(0.79, 1.26)
Model C	.23			.23		
PA		-0.78	(-1.04, -0.52)		-0.78	(-1.05, -0.52)
ABSI^2		0.07	(-0.12, 0.26)		0.09	(-0.10, 0.28)

CI: confidence interval. BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index. Cardiometabolic risk score calculated as the sum of the z-scores of triglycerides, inverse of high density lipoprotein cholesterol, homeostatic model assessment of insulin resistance, and systolic blood pressure.
Physical activity as measured by NL-1000 accelerometers.
%Total and %Central fat as measured by dual energy X-ray absorptiometry.
Adjusted for age and oral contraceptive use.
*Standardized beta coefficients.

APPENDIX C

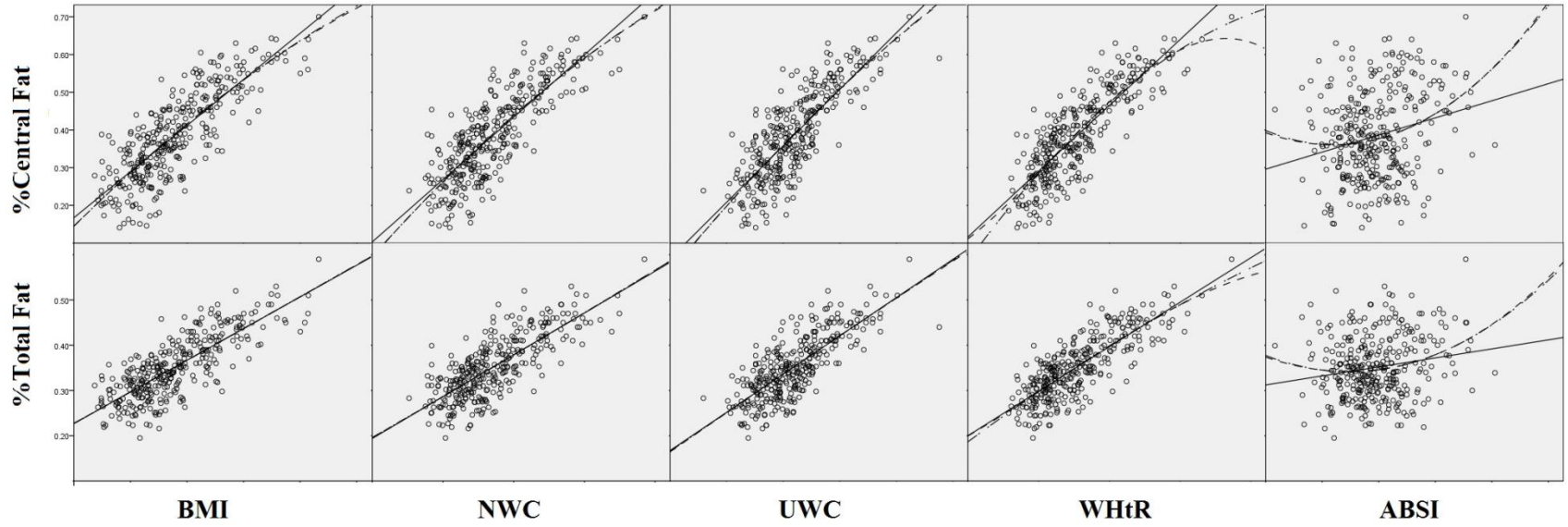

Figure 1. Curve estimation regression of anthropometric measures of body fatness and DXA measured body fat.
%Total Fat: percent total fat. %Central Fat: percent central fat. BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index.

APPENDIX D

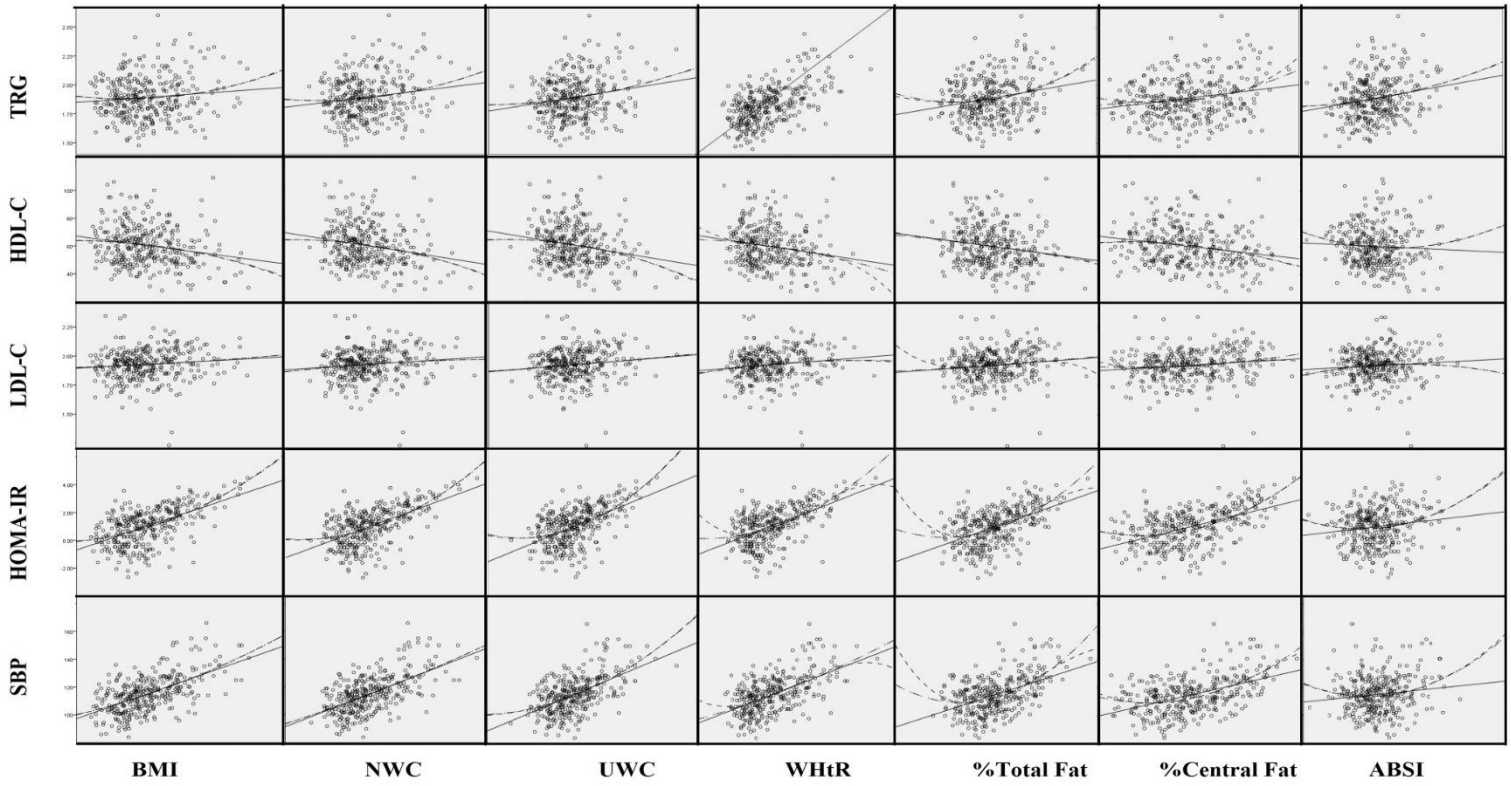

Figure 2. Curve estimation regression of different body fat measure and cardiometabolic risk factors.
%Total Fat: percent total fat. %Central Fat: percent central fat. BMI: body mass index. WC-N: narrowest waist circumference. WC-U: umbilical waist circumference. WHtR: waist circumference-to-height ratio. ABSI: a body shape index. SBP: systolic blood pressure. HOMA-IR: homeostatic model assessment of insulin resistance. HDL-C: high density lipoprotein. TRG: triglyceride.