Central Blood Pressure Regulation in Relation to Obesity in Youth

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Abstract

Introduction Measures of central blood pressure (BP) are hypothesized to be positively associated with obesity status in youth. However, few studies have addressed this topic with a large sample size and wide range of BMI values.

Methods A total of 310 participants (males/females =151/159) aged of 8 to 18 years old (mean±SD: 12.8±2.7 years) were recruited. Height (cm) and weight (kg) were measured using a wall-mounted stadiometer and an electric scale. Body mass index (BMI) was calculated (kg/m^2) and obesity status was determined using age – and sex- derived BMI percentile (BMI%) with the following categories: normal weight (NW) represented as $<85^{th}$ BMI percentile; overweight/obesity (OW/OB) represented as between 85^{th} to < 1.2 times the 95^{th} BMI percentile); severe obesity (SO) represented as ≥ 1.2 times the 95^{th} BMI percentile. Dual energy X-ray absorptiometry (DXA) was used to measure body composition. Brachial systolic (SBP) and diastolic (DBP) blood pressure was measured with an automated cuff. Central BP was obtained from SphygmoCor MM3 systems, which utilizes applanation tonometry to derive radial-aorta SBP (r-a SBP), radial-aorta DBP (r-a DBP), carotid-aorta SBP (c-a SBP), and carotid-aorta DBP (c-a DBP). Central BP measures were compared across obesity groups using ANCOVA with post-hoc Tukey HSD, adjusted for age, Tanner stage, sex, and race, with further adjustment of height for brachial BP. Unadjusted Pearson correlations examined the relationship between central BP measures with obesity (BMI, BMI%, body fat (%), visceral fat mass (kg)). Linear regression analyses examined the association between body fat (%) and visceral fat mass (kg) with brachial and central SBP and DBP after adjusting for age, Tanner stage, sex, and race, with height included for brachial BP.

Results There were 120 NW, 89 OW/OB, and 99 SO participants. Body fat (%) was significantly different ($p<0.001$) among all obesity groups: NW (25.1±6.1 %), OW/OB (39.5±7.2 %), SO (48.0±4.9 %). Brachial SBP (bSBP), r-a SBP, and c-a SBP significantly increased ($p<0.001$ all) with increasing obesity status. BMI was significantly correlated ($p<0.001$ all) with bSBP ($r=0.64$), r-a SBP ($r=0.57$), and c-a SBP ($r=0.52$). BMI%, body fat (%), and visceral fat mass (kg) were also all significantly correlated to all brachial and Central BP measures. In multiple regression models, higher values of body fat (%) were significantly associated (all $p<0.001$) with higher brachial ($r=0.66$) and central SBP (r-a $r=0.59$) (c-a $r=0.55$) as well as brachial ($r=0.44$) and central DBP (r-a $r=0.42$) (c-a $r=0.46$). Higher values of visceral fat mass (kg) were significantly associated (all $p<0.001$) with higher brachial ($r=0.61$) and central SBP (r-a $r=0.60$) (c-a $r=0.55$) as well as brachial ($r=0.39$) and central DBP (r-a $r=0.42$) (c-a $r=0.44$). Older age was significantly associated with higher r-a SBP ($r=0.59$. $p<0.001$) and c-a SBP ($r=0.55$, $p<0.01$).

Conclusion Central BP, regardless of measurement site, is highly associated with Obesity status (BMI, BMI%, body fat (%), and visceral fat mass (kg)) and hypertension status among youth.

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List of Abbreviations

AiX: augmentation index

bDBP: brachial diastolic blood pressure

bDBP%: brachial diastolic blood pressure percentile

bf%: body fat percentage

BMI: body mass index

BMI%: body mass index percentile

BP: blood pressure

bSBP: brachial systolic blood pressure

bSBP%: brachial systolic blood pressure percentile

c-a: carotid to aorta

CDC: Center for Disease and Control and Prevention

CVD: cardiovascular disease

cIMT: carotid intimal medial-thickness

c-r: carotid to radial

DBP: diastolic blood pressure

DXA: dual X-ray absorptiometry

kg: kilograms

LVM: left ventricle mass

MAP: mean arterial pressure

m^2 = squared meters

mm: millimeters

mmHg: millimeters of mercury

NW: normal weight

OB: obesity

OW: overweight

PWA: pulse wave analysis

PWV: pulse wave velocity

r-a: radial to aorta

SBP: systolic blood pressure

SO: severe obesity

SV: stroke volume

VAT: visceral fat mass (kg)

Chapter 1: INTRODUCTION

From 2011 to 2014, the prevalence of obesity among youth aged 2 to 19 years old was 17%, and the prevalence of severe obesity was 5.8% (Ogden, et al., 2016). Additionally, its estimated that between 3 to 5% of youth have hypertension (Falkner, 2010; Obarzanek, et al., 2010; Thompson, Dana, Bougastsos, Blazina, & Norris, 2013). Hypertension has been identified as an outcome related to childhood obesity, with an increased risk of hypertension concurrent with increased body mass index (BMI) among youth (Tu, et al., 2011). Specifically, obese youth were found to have a 3- to 4-fold higher risk of hypertension compared to normal weight youth (Sorof & Daniels, 2002). Overall, obesity has been recognized as a major cause of high blood pressure (BP) and hypertension in youth, and the combination of obesity and hypertension is recognized as a pre-eminent cause of cardiovascular events in adulthood (Langsberg, et al., 2013).

Numerous studies have compared the association between obesity and brachial artery BP, but few studies have investigated the association between obesity and central blood pressure (central BP) among youth (Kolade, et al., 2012; Langsberg, et al., 2013; Re, 2009; Sorof & Daniels, 2002; Tu, et al., 2011). Central BP is the pressure of blood within the aorta and is measured in millimeters of mercury (mmHg). The heart, kidneys, and major arteries supplying the brain are exposed to central BP rather than brachial BP (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014). Additionally, through multivariate analysis and simple correlation, central BP has been found to be more strongly associated to surrogates of cardiovascular disease (CVD) and future cardiovascular events in adults in comparison to brachial BP (Pini, et al., 2008; Wang, et al., 2009; Roman M. J., et al., 2009; Roman M. J., et al., 2007; Vlachopoulos, Aznaquridis, & Stefanadis, 2010).

Central systolic BP (SBP) and diastolic BP (DBP) can be measured invasively using a pressure-sensing catheter or calculated noninvasively via applanation tonometry (SphygmoCor, AtCor Medical, City, Country). Central SBP and central DBP are estimated by pulse wave analysis (PWA) at either the radial or carotid pulse via a stylus tonometer (i.e., pressure transducer). Since brachial mean arterial pressure (MAP) and DBP values do not vary as markedly across the arterial tree, carotid pulse waves are calibrated to brachial MAP and DBP values (Kroeker & Wood, 1995). Radial values are calibrated to brachial SBP and DBP and have been found to have similar errors as brachial BP when compared to invasive measurements (O'Rourke & Adju, 2012; Shih, Cheng, Sung, Hu, & Chen, 2011). Pulse waves recorded from either peripheral site are used to estimate central aortic pressure using a validated generalized transfer function (Van Bortel, et al., 2012; Miyashita, 2012). Augmentation index (AiX) is also estimated by PWA, and represents the percentage of the pulse pressure due to backward traveling waves within the central arteries (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014).

Previously, central BP was found to be higher in healthy obese adults when compared to healthy normal weight adults (Kolade, et al., 2012). This study by Kolade et al, however, did not asses central BP in SO youth. Utilizing our SO group, our study set out to fill this gap in the literature. BMI has also previously been associated with both brachial and central BP in healthy adults (Kolade, et al., 2012), but these relations in youth are missing. The first aim of this study was to examine relationships between obesity with both brachial BP and Central BP among youth. This cross-sectional study allowed us to examine differences in BP across three obesity groups; Normal weight

(NW), Overweight/ Obesity (OW/ OB), and Severe Obesity (SO). Another aim of this study was to determine the association BMI, BMI percentile (BMI%), body fat percent (bf%), and visceral fat mass (kg) (VAT) have on measures of central BP.

Chapter 2: LITERATURE REVIEW

Blood pressure

Arterial BP is the force that drives the flow of blood through the vascular system in the human body as the heart contracts (i.e., systolic pressure) and relaxes (i.e., diastolic pressure). The human body requires a consistent flow of blood to perfuse vital organs and to transport nutrients, hormones, and metabolic waste products. Blood flow is calculated as dividing the pressure gradient generated from the heart's left ventricle by the resistance within the vasculature of the arterial walls.

Brachial Blood Pressure

Blood pressure measured at the brachial artery by means of a sphygmomanometer is widely accepted as an important predictor of future cardiovascular risk. Brachial BP has been performed for over 100 years and was initially used by life insurance companies to determine future CVD risk among asymptomatic individuals (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014)

Measurements of brachial BP are routinely used to clinically diagnose hypertension. Using brachial SBP percentiles (bSBP%) based on age, sex, and height norms, youth are considered normotensive ($<90^{th}$ percentile), pre-hypertensive ($\geq 90^{th}$ percentile to $< 95^{th}$ percentile), or hypertensive ($\geq 95^{th}$ percentile) (CDC, 2015). Although central BP can be used as assessment of BP, it is currently used primarily for research purposes only.

Central Blood Pressure

Central BP is measured at the central arteries, such as the aorta. Measurements can be invasively obtained through pressure-sensing cardiac catheterization into the aorta. Central BP can be non-invasively estimated via pressure waveforms obtained at distal

locations to the aorta (e.g., carotid, radial, and femoral) (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014).

To measure central BP non-invasively, a tonometer is used to record pressure waves. A pressure wave is generated by the summation of a forward traveling pulse wave from the heartbeat and a backward traveling pulse wave from disturbances along the vessel. Through an algorithm of distance (cm) between the person's sternum and radial pulse, central BP is estimated in mmHg. The summated pulse wave can also be analyzed for AiX, which is the influence of backward traveling wave or arterial resistance (Marcus, 2016).

Currently there are no hypertension guidelines or categories that use central pressure parameters. However, the Strong Heart study found that a central pulse pressure (i.e., difference between systolic and diastolic pressures) of greater than or equal to 50 mmHg was associated with increased risk of future cardiovascular events (e.g., heart attack or stroke) (Roman, et al., 2007). A study by Elmenhorst and colleagues evaluated normal central BP values in youth between 8 to 22 years old and observed that females have central BP between 91.2 to 100.7 mmHg, while males have central BP values between 90.0 to 110.5 mmHg (Elmenhorst, et al., 2015).

Non-invasive measurement of central BP are typically calibrated using the subject's brachial SBP and DBP, However, research has found that this method of calibration characteristically underestimates true invasive brachial BP and falsely records low estimates of central BP (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014). Regardless, recent data has demonstrated that errors in the estimated central BP

are equivalent to errors in manually auscultating brachial BP (O'Rourke & Adju, 2012; Shih, Cheng, Sung, Hu, & Chen, 2011).

Associations between brachial and central blood pressure

Brachial and central BP essentially measures the same physiological occurrence. However, both techniques can derive different values of blood pressure, with central BP commonly lower than brachial BP. A potential rationale to explain the underestimation in central BP is due to increased vessel size of the aorta (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014). Central BP can be also lower due to arterial stiffening in the peripheral arteries (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014).

In addition to measuring central SBP and DBP, augmented pressure is another parameter that can be obtained during a PWA assessment. Augmented pressure evaluates the degree of amplified BP due to vessel resistance. The ability of central BP to differentiate pressure values due to contractility or blood volume versus peripheral resistance could potentially allow for enhanced diagnostic potential in the medical treatment of hypertension.

The use of both brachial and central BP concurrently to determine an individual's hypertension status increases risk stratification for hypertension and future CVD events. It has been demonstrated that when adults were stratified into hypertension status (e.g., normal, pre-hypertension, and hypertension) by brachial guidelines, individuals were observed to have considerable status overlap in terms of central BP values. Seventy percent of individuals who had normal to high brachial blood pressure, had similar aortic pressures to those with stage 1 hypertension (McEniery, et al., 2008). This can lead insufficient medical treatment.

Central BP can be assessed with similar ease as the brachial BP; however, the assessment of central BP is missing standardization within the methods of operator index score. Recent evidence suggests that central BP is a stronger predictor of cardiovascular risk. Since, the heart, kidneys, and major arteries supplying the brain are exposed to central rather than brachial BP, central BP is more closely related to CVD events (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014).

Obesity and Blood Pressure

Currently around 3% of youth are diagnosed hypertensive (Falkner B. , 2010). Youth are typically screened for BP at routine clinic visits and high BP on 3 consecutive visits may give reason for diagnosis (Falkner B. , 2010). Obesity is associated with both hypertension and risk of CVD. Risk of hypertension increases across the BMI spectrum (Sorof & Daniels, 2002). It has been observed that obese youth are at a 3- to 4-fold higher risk for hypertension then non-obese children (Sorof & Daniels, 2002).

The Center for Disease and Control and Prevention (CDC) uses BMI percentile to classifies obesity status as underweight ($<5^{th}$ percent), healthy weight ($\geq5^{th}$ to 85^{th} percentile), overweight ($\geq85^{th}$ to $<99^{th}$ percentile), or obesity ($\geq95^{th}$ percentile) (Center for Disease Control and Prevention, 2015). However, experts in the field of pediatric obesity have recently started using the following cutoff values for obesity status: NW ($<85^{th}$ percentile), OW/OB (85^{th} to <1.2 X the 95^{th} percentile), and SO (1.2 X the 95^{th} percentile) (Ryder, et al., 2015; Kelly A. S., 2014; Flegal, et al., 2009).

Recent findings suggest that obesity related hypertension is characterized by dysfunction of the sympathetic nervous system, renin-angiotensin system, and sodium retention. From a pathophysiology standpoint, obesity has been found to predispose

individuals to hypertension by increasing blood flow, vasodilation, and cardiac output. (Re, 2009).

In healthy adults, BMI has been associated with brachial ($r=0.3$, $p<0.001$) and central BP ($r=0.29$, $p<0.001$) (Kolade, et al., 2012). However, BMI was not associated with brachial and central BP among individuals with diabetes, coronary artery disease, or end stage kidney disease (Kolade, et al., 2012). These findings suggest that, among asymptotic and healthy individuals, central and brachial BP are both associated with BMI in a similar fashion. Another study compared obesity, stroke volume (SV), pulse wave velocity (PWV), and central BP and found that central BP was greater in obese children aged 5 to 15 years old (Castro, et al., 2016). In this study (Castro et al., 2016) increased central BP was more closely associated to SV than with PWV. These findings suggest increased blood pressure in obese children may more likely be derived from issues in SV and left ventricular contractility rather than peripheral resistance.

Risk of Cardiovascular Disease and Blood Pressure

Hypertension is considered a strong and modifiable risk factor of CVD (Gu, Burt, Paulose-Ram, Yoon, & Gillum, 2008). The relationship between brachial BP and CVD are linear, as well as consistent, and independent of other risk factors.

In adults, central BP has been observed to be more related to future cardiovascular events then brachial BP in healthy, asymptomatic individuals (Roman, et al., 2007). central BP has been closely associated with cardiovascular events and CVD markers such as: heart failure, stroke, kidney disease, carotid intimal medial-thickness (cIMT), left ventricle mass (LVM), heart rate variability, coronary artery disease, cerebrovascular disease, renal insufficiency, left ventricle hypertrophy, atrial fibrillation, PWV, and AiX

(Pini, et al., 2008; McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014; Ryder, et al., 2015; Re, 2009; Lurbe, et al., 2012; Pichler, et al., 2015).

In summary, BP is the force that drives the flow of blood through the vascular system in the human body as the heart contracts. Brachial artery BP is currently used to determine an individual's hypertension status as it is widely accepted as an important predictor of future cardiovascular risk. Recently central BP has been observed to be more related to future cardiovascular events then brachial BP in healthy adults, however, currently there are no hypertension guidelines or categories that use central pressure parameters. Both brachial and Central BP measure the same physiological occurrence and have been associated to BMI in adults. Obesity is related to hypertension and has been shown with brachial BP in youth, however much evidence is missing from the literature between obesity and central BP in youth and should be further examined.

Chapter 3: METHODS

Study Design and Participants

A sample of females (n=159) and males (n=151) between the ages of 8 to 18 years old (mean±SD: 12.8±2.7 years) were used in this cross-sectional analysis. Participants were recruited from the University of Minnesota Masonic Children's Pediatric Weight Management clinic (participants with OW/OB and SO) and the primary care pediatric clinics at the University of Minnesota as part of a cross-sectional cardiovascular risk across the BMI spectrum study in youth. Participants were excluded for the following reasons: obesity due to a genetic cause, weight loss surgery, BP medication use, illness or injury, type 1 diabetes, history of hypercholesterolemia, chronic kidney disease/end-stage renal disease, Kawasaki disease, autoimmune inflammatory diseases, or congenital heart disease. The University of Minnesota IRB board approved the study protocol and informed consent was obtained from each participant and their parent or guardian.

Anthropometrics, Body Composition Assessments, and Pubertal Maturation.

All testing was performed at the University of Minnesota with the participant in a fasted-state for at least 12 hours prior to the visit. Height and body mass were measured using a wall-mounted stadiometer and an electric scale. Each measure was collected 3 times, and the average was recorded. Body Mass Index was calculated using body mass in kilograms (kg) divided by height in squared meters (m^2). Participants obesity status was determined by BMI% as Normal weight (NW) (<85th percentile), Overweight/ Obesity (OW/OB) (≥ 85th - < 1.2 times the 95th percentile), or Severe Obesity (SO) (≥ 1.2 times the 95th percentile) participants. Dual X-ray absorptiometry (DXA) (General Electronic Medical Systems, Madison, WI) using enCore^{TM} software (platform version

16.0, GE systems) was used to determine body composition variables including body fat percent (bf%). A trained nurse determined pubertal maturation using tanner stages (1-5 scale) (World Health Organization, 2010).

Brachial Blood Pressure and Heart Rate

After resting in a seated position for at least 10 minutes, heart rate and BP were obtained with an automated BP cuff (COLIN Medical Instruments, Escondido California) measured 3 times with 3-minutes between trials. The average of the final two BP measurements was used as BP. Brachial SBP percentiles were determined based on age, sex, and height (The Fourth Report, 2004)

Pulse Wave Analysis and Pulse Wave Velocity

Following 15 minutes of rest in the supine position, PWA measurements were taken at the right radial and right carotid artery using applanation tonometry with SphygmoCor ®MM3 systems (AtCor Medical, Sydney Australia) (Laurent, et al., 2006; Wilkinson, et al., 2000). Collected waveforms were calibrated and scaled using each subject's individual resting brachial BP. After acquiring arterial waveforms, a validated generalized transfer function was used to estimate the corresponding central (aortic) BP (Van Bortel, et al., 2012; Croymans, et al., 2014; Laurent, et al., 2006; Miyashita, 2012). Central SBP and DBP were estimated using radial to aorta (r-a) and carotid to aorta (c-a) pulse waves. PWA was used to estimate the AiX at both the radial and carotid pulse. Augmentation index was defined as augmented pressure (P2-P1) expressed as a percentage of central pule pressure. Augmentation index is influenced by heart rate so was normalized for a heart rate of 75 beats per minute (Wilkinson, et al., 2000).

Carotid to radial (c-r) PWV was determined using SphygmoCor ®MM3 systems by sequentially recording electrocardiographic-gated carotid and radial artery waveforms suing applanation tonometry. Distance from the carotid sample site to the radial artery site was measured in millimeters (mm). The time interval (in seconds) between onset of radial and carotid waveforms was determined.

Statistical Analysis

Data was stored on a security-enabled server (HIPAA-compliant, limited access). R software (R version 3.2.3. Released 2015) and IBM SPSS Statistics 23 (IBM Corp. Released 2016, IBM SPSS Statistics for Windows, Version 23, Armonk, NY: IBM Corp) were used to conduct statistical analyses.

To determine differences between obesity status, analysis of variance (ANOVA) was used to compare age, tanner, sex, and race across obesity groups (Table 1). Physical characteristic variables height, weight, BMI, BMI%, waist circumference, and heart rate, body composition variables such as total body bone mineral content (BMC), total lean mass, total fat mass, bf%, visceral fat mass (VAT), android lean and fat mass, gynoid lean and fat mass, and BP variables brachial, r-a, and c-a (Table 3) were compared across obesity status using analysis of covariance (ANCOVA), with post-hoc Tukey HSD. Variables were adjusted for age, tanner stage, sex, and race. Brachial BP was also adjusted for height.

Unadjusted Pearson correlation were used to determine strength and direction of the linear relationship between BMI, BMI%, Bf%, VAT (kg) and BP measures using all participants and broken down by sex. Multiple linear regression models were used to examine the relationship between central BP measures with adiposity; these models were

adjusted for age, tanner stage, sex, and race. Brachial BP was additionally adjusted for height.

Chapter 4: RESULTS

Physical and Demographic characteristics of participants

Determined by BMI%, there were 120 NW, 89 OW/OB, and 99 SO participants. Participant's physical and demographic characteristics by weight status are shown in Table 1. There were no significant differences in participants age across all obesity groups. Tanner stage was significantly lower ($p=0.01$) in the NW group compared to the SO group, while the OW/OB group was not different from either group. There were significantly more ($p<0.01$) males (58%) in the NW group compared to the SO group (38%.), while the OW/OB group (48%) was not different than either group. There were significantly more ($p<0.001$) white participants in the NW group compared to both OW/OB and SO groups. BMI significantly increased ($p<0.001$) with greater obesity status.

Body Composition characteristics of participants

Participants body composition characteristics by weight status are displayed in Table 2. As expected, participant's bf% percentage significantly increased ($p<0.001$) across obesity status; NW (25.1±6.1%), OW/OB (39.5±7.2%), SO (48.0±4.9%), respectively. Total lean mass, total fat mass, bf%, VAT, android lean and fat mass, gynoid lean and fat mass were found to be significantly increased ($p<0.001$ all) with greater obesity status. Total body BMC was not significantly different between any groups ($p=0.4$), and remained not significant after adjusting for weight ($p=0.42$).

Blood Pressure and Vascular characteristics of participants

Participant's blood pressure characteristics by weight status are shown in Table 3. Brachial SBP (bSBP) and bSBP% significantly increased ($p<0.001$) across obesity groups, while brachial DBP (bDBP) and bDBP percentile (bDBP%) significantly

increased in the SO group compared to both the NW and OW/OB groups. Brachial MAP significantly increased ($p<0.001$) across all three groups.

Radial-aortic SBP significantly increased ($p<0.001$) across each obesity group. Radial-aorta DBP was significant higher ($p<0.001$) in the SO group compared to both NW and OW/OB groups, with no differences between the NW and OW/OB groups. Radial-aorta AiX was significantly higher in the SO group compared to the NW group, while the OW/OB group was not significantly different from either group.

Carotid measures identified c-a SBP significantly increased ($p<0.001$) across each obesity group. Carotid-aorta DBP was significantly higher ($p<0.01$) in the SO group compared to the NW group, while the OW/OB group was not different from either group. Carotid-aorta AiX was significantly higher ($p<0.01$) in the NW group compared with OW/OB and SP groups, but no statistical difference was identified between the OW/OB and SO groups.

Radial-aorta SBP was significantly lower ($p<0.01$) than bSBP and c-a SBP within each obesity group. Carotid-aorta SBP was not significantly different than bSBP within any obesity group. PWV was not significant different ($p=0.98$) between any of the obesity groups.

Blood pressure and Obesity correlations of participants

Pearson correlation between BMI and BP variables can be found in Table 4. BMI was significantly (all $p<0.0001$) correlated with bSBP/ DBP, r-a SBP/ DBP and c-a SBP/ DBP. Correlations between BMI% and BP variables can be found in Table 5. BMI percentile significantly (all $p<0.01$ at least) correlated with bSBP/ DBP, r-a SBP/ DBP, and c-a SBP/ DBP. Correlations between bf% and BP variables can be found in table 6.

Bf% significantly (all $p<0.01$ at least) correlated with bSBP/ DBP, r-a SBP/ DBP, and c-a SBP/ DBP. Correlations between VAT (kg) and BP variables can be found in table 7. Visceral fat mass significantly (all $p<0.01$ at least) correlated with bSBP/ DBP, r-a SBP/ DBP, and c-a SBP/ DBP.

Multiple Linear Regression to predict Blood Pressure Measurements

Tables 8 and 9 show linear regression analyses examining the association between bf% and VAT with brachial and central SBP and DBP. Higher values of bf% and VAT were significantly associated with higher brachial and central SBP and DBP ($p<0.001$ all). Higher values of age significantly associated to higher r-a and c-a SBP ($p<0.001$ and $p<0.01$, respectively).

Chapter 5: DISCUSSION

The purpose of this study was to compare relationships between obesity status and measures of brachial and central BP. Obesity status, determined by BMI%, classified participants as: NW, OW/OB, or SO (Flegal, et al., 2009). Major findings in this study determined that both adjusted-brachial and adjusted-central SBP differences can be found across all obesity groups. BMI, BMI%, bf%, and VAT were correlated to all measures of unadjusted-BP. Body fat (%) and VAT significantly predicted all measures of adjusted-BP. These study findings suggest a strong relationship between brachial and central BP across obesity status.

Brachial BP and Obesity

Our study detected significant increases in brachial SBP with each increase in obesity status. Like other studies, brachial SBP was significantly higher with higher obesity status and both strongly and positively associated with BMI and BMI% (Koebnick, et al., 2013; Lo, et al., 2013; Castro, et al., 2016; Fernandes, et al., 2011; Chiolero, Cachat, Burnier, Paccaud, & Bovet, 2007; Salvadori, et al., 2008; McGavock, Torrance, McGuire, Wozny, & Lewanczuk, 2007; Lu, et al., 2013; Moura, Silva, Ferraz, & Rivera, 2004; Junaibi, Abdulle, Sabri, Hag-Ali, & Nagelkerke, 2013; Zhang & Wang, 2012). This study by Koebnick recognized that prevalence of hypertension was best predicted by a BM8I% $\geq 94^{th}$ percentile and that SO and OB youth are 10-fold and 4-fold more likley to be hypertensive compared to NW youth. Agreeing with this study, Chirita-Emandi and company found the strongest determinant of hypertension to be BMI% in Romanian youth. (Chirita-Emandi, Puiu, Gafencu, & Pienar, 2013)

Others have recognized that the strongest risk factor for primary hypertension in children of all ages and sex is elevated BMI (Thompson, Dana, Bougastsos, Blazina, &

Norris, 2013; Falkner, et al., 2006; Chiolero, Cachat, Burnier, Paccaud, & Bovet, 2007; Liao, et al., 2009; Langsberg, et al., 2013). These findings are important as increases in obesity, brachial BP and hypertension status in both youth and adults are recognized as indicators of future CVD (Langsberg, et al., 2013; PS, 2002; Neaton, Kuller, Stamler, & Wentworth, 1995; Stamler, Stalmer, & Neaton, 1993; Wilson, D'Agostino, Sullivan, Parise, & Kannel, 2002). By better understanding these risks obese youth face may help us to better screen, prevent, and treat hypertensive youth.

Our study found bDBP was significantly higher in the SO group compared to both the NW and OW/OB groups, while there were no differences between the NW and OW/OB groups. This is comparable to previous findings that found no differences in bDBP between NW (mean BMI% = 64.1) and OW (mean BMI% = 98.5) healthy youth, p=0.45 (Castro, et al., 2016). These findings may suggest that only SO youth show signs of high diastolic values compared to NW or OW/OB. This is consistent with reports that SO youth have a much more adverse cardiometabolic risk factor profile (Kelly A. S., 2014; Freedman, Mei, Srinivasan, Berenson, & Dietz, 2007; Calcaterra, et al., 2008; Ice, Murphy, Cottrel, & Neal, 2011; Weiss, et al., 2004). Other research has found that obesity related hypertension appears to be characterized by isolated systolic hypertension in youth and may help explain these findings. (Sorof & Daniels, 2002; Koebnick, et al., 2013; Dorresteijn, Visseren, & Spiering, 2012).

Body fat (%) is another determinant of obesity in youth, although it is not as commonly used to define obesity status (Fernandes, et al., 2011; Taylor, Jones, Williams, & Goulding, 2002; McCarthy, Cole, Fry, Jebb, & Prentice, 2006; Cole, Bellizzi, Flegal, & Dietz, 2000; Fernandes R. , et al., 2010; Neovius & Rasmussen, 2008). Our study

found bf% significantly predicted and correlated to both brachial SBP and DBP. Like our findings, previously bf% determined with DXA was found to be significantly higher with higher obesity status and associated to both brachial SBP and DBP in youth (Fernandes R. A., et al., 2011). A dose-response effect has also been observed and described between brachial BP and bf% when measured by skin-folds in adults (Williams, et al., 1992).

Another obesity measure, VAT has been related to adverse cardiovascular events (Britton, Massaro, Murabito, & Kreger, 2013), insulin resistance (Fox, et al., 2007; Needland, et al., 2012; McLaughlin, Lamendola, Liu, & Abbasi, 2011), higher atherosclerotic risk profile (Needland, et al., 2012) and increased cytokine production (Cartier, et al., 2009). These relations all suggest a link between VAT and CVD, as well as helps us understand where fat mass is being stored. Our study found VAT significantly increased with increasing obesity status. VAT also significantly predicted and correlated to all measures of brachial SBP and DBP. In youth, visceral fat determined by DXA levels above the mean was positively associated with brachial SBP (Kelly, et al., 2014). In adults, visceral fat determined with MRI had been directly related to mean BP fitting a model that demonstrated for every 1 kg increase in visceral fat a 10 mmHg of mean blood pressure was found (Sironi, et al., 2004). Major findings from this Sironi were that hypertensive men had significantly more visceral fat then non-hypertensive with approximately the same total fat (Sironi, et al., 2004). Increased VAT determined by DXA has also been found to associate with incident hypertension in adults (Chandra, et al., 2014). A 12-week low calorie diet in obese hypertensive women found decreases in both visceral fat (determined by a computer tomographic section at the umbilicus) and

MAP to be correlated, however MAP was not correlated with decreased in body weight or BMI (Kanai, et al., 1996). These findings are like ours and help understand the relationships between BP and body composition measures outside of normative based measures such BMI and BMI%.

Central BP and obesity

Central SBP measures (r-a and c-a) significantly increased with each increase in obesity status. Previous research found healthy OB youth have increased r-a SBP compared to their NW counterparts (Castro, et al., 2016). While this study by Castro used BMI-z scores to determine obesity status, our current study added to the literature by further breaking down and defining more specific obesity groups (i.e NW, OW/OB, SO). In adults, Pichler found r-a SBP increased from NW to OW to OB individuals, however the risk of SO individuals were not analyzed (Pichler, et al., 2015). Another study first separated individuals into high or low BP groups and found those with significantly higher central SBP also had significantly higher BMI (Radchenko, Torbas, & Sirenko, 2016).

We determined r-a and c-a SBP were significantly and positively associated with BMI (r=.57 and r=.52, respectively). In healthy adults, Kolade (r=.29), Radchenko (r=.45), and Pichler (r=.17) also found r-a SBP to be significantly and positively associated to BMI (Kolade, et al., 2012; Radchenko, Torbas, & Sirenko, 2016; Pichler, et al., 2015). Our results add to the literature by demonstrating this association between central SBP and BMI in youth, reporting stronger correlations then previously found in adults.

Central (r-a and c-a) DBP was significantly increased in SO individuals compared to NW. R-a DBP was also significantly increased in the SO group compared to OW/OB group. These findings follow a similar pattern to brachial DBP results where the biggest changes come between NW and SO participants. Previously in youth there were no r-a DBP differences found between NW and OB youth (Castro, et al., 2016). In adults r-a DBP has been found to significantly increase between OW/OB compared to NW individuals (Pichler, et al., 2015). As previously mentioned, SBP variables may be more indicating of hypertension status or risk of CVD. Currently there is little documentation regaridng central DBP and obesity status, this study helps to fill gaps these in the literature.

To our knowledge, this is the first study to analyze bf% and VAT against central BP in youth. As previosly mentioned, these variables are used to determine and describe obesity status as well as are related to CVD. Our study found bf% and VAT both signifcantly predicted and correlated to all measured of central SBP and DBP. These findings followed similar relationships as to brachial BP and help us understand the connections between how much fat and where its stored in comparision to central BP in youth.

Brachial and Central BP

As presented in this study, central SBP measures followed matching patterns to brachial SBP across obesity groups. Although no formal analysis was run between location sites, significant differences between obesity groups were the same regardless of SBP measurement location. These similar relationships are important and hold implications as increased central and brachial BP relate to CVD and CV events

(Frankline, McEniery, Cockcroft, & Wilkinson, 2014; McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014).

Although brachial and central BP measures followed similar patterns between obesity groups, r-a SBP was significant lower than both bSBP and c-a SBP within each group. This is consistent with other findings and from a physiological perspective, SBP varies throughout the arterial tree as central SBP has been found to be lower than corresponding bSBP (McEniery, Cockcroft, Roman, Franklin, & Wilkinson, 2014). Additionally, non-invasive measurements of central BP such as SphygmoCor have previously shown to underestimate central BP giving an additional reason central SBP was lower than brachial SBP (O'Rourke & Adju, 2012).

PWV and Obesity

The differences in BP between obesity groups appear to occur without concurrent differences in arterial stiffness, as measured by PWV. Overall, there were no observed differences in PWV across all three obesity groups. PWV has previously been negatively related to BMI% (Lurbe, et al., 2012). Although PWV differences among NW and OB youth were previously observed in research conducted by Castro and colleagues such discrepancies compared to this current study may be due to differences in the locations used for measuring PWV (Castro et al., 2016). Castro and colleagues measured PWV using femoral-carotid, while in the present radial-carotid sites were used. Other studies have found that PWV has greater associations to age, height, and BP rather than weight (Reusz, et al., 2010; Elmenhorst, et al., 2015). Our sample did not have differences in age, which may explain a lack of a difference in PWV across obesity groups.

AiX and Obesity

We reported r-a AiX increased across obesity groups, while c-a AiX decreased. Greater AiX values indicate increased wave reflection and a potential earlier return of the reflective wave due to increased PWV (i.e., increased arterial stiffness) or closer reflection sites (Castro, et al., 2016). Findings by Castro, reported OB youth had significantly lower r-a AiX than their NW counterparts. Castro's findings are similar to our c-a AiX results and oppose our r-a AiX findings. Based on these mixed results, AiX should be further investigated in youth across the obesity spectrum.

Strengths and Limitations

A strength of this study was the sample population. The wide range of BMI values and groups ranging from NW to SO allowed for detecting small changes between youth who for example may be OW/OB compared to SO. Although we used established cut off ranges to determine obesity status (Flegal, et al., 2009; Kelly A. S., 2014), we also compared body composition data from DXA in each group to further solidify the relationship with obesity. Including relationships between bf%, visceral fat and BP variables allowed us to take a closer look at individual data on each participant outside of normative classifications such as BMI and BMI%.

Another strength in this study was multiple BP measurement locations. Compared to other central BP studies relating to obesity, to our knowledge ours was the only to present SBP and DBP findings from both r-a and c-a locations. Comparing these locations is important to help us understand the change in BP across the arterial tree with changes in obesity status in youth. We were also able to compare central BP results with

the much further studied brachial BP to determine similarities and differences between the two locations.

A limitation is the lack of validated methods for estimating central BP, such as SphygmoCor, in youth. Currently, SphygmCor is not validated for central BP in youth. Adding to this limitation, SphygmoCor and applanation tonometry can be operator dependent and rely on transfer functions. SphygmoCor systems also use brachial BP in calibration which may limit or confound their estimation. Despite these limitations, central BP has been validated in adults and r-a BP has been found to have similar errors to brachial BP (O'Rourke & Adju, 2012; Shih, Cheng, Sung, Hu, & Chen, 2011).

Another limitation is there are no current central BP categories based on increased risk of disease in adults and youth as there are with brachial BP. Current references are values based on age, sex, and brachial BP, but these would have little use in a clinical setting (Herbert, Cruickshank, Laurent, & Boutouyrie, 2014).

Future Studies

Moving forward it would be helpful to further examine the potential causes of increased central BP in obese youth in the context of a longitudinal study as this study focused on analyzing cross-sectional relationships between central BP and BMI. Future studies are needed to validate central SBP methods in youth. Research should focus on collecting normative data and determining appropriate and clinically relevant central blood pressure categories. Once central BP values are found to determine hypertension status, our current study could include hypertension status determined by central BP as an analysis.

Chapter 6: Conclusion

In conclusion, this study was designed to compare relationships between obesity status and measures of brachial and central BP. Brachial BP is currently used to determine an individual's hypertension status as it is widely accepted as an important predictor of future cardiovascular risk. Recently central BP has been observed to be more related to future cardiovascular events then brachial BP in healthy adults, however, currently there are no hypertension guidelines or categories that use central pressure parameters. Both brachial and central BP measure have been associated to BMI in adults, however, much evidence is missing from the literature between obesity and central BP in youth and needed to be further examined.

This study determined that both adjusted-brachial and adjusted-central SBP differences can be found across all obesity groups. Body mass index, BMI%, bf%, and VAT were correlated to all measures of unadjusted-BP. Body fat percentage significantly predicted all measures of adjusted-BP. The main finding from this study suggests a strong relationship between brachial and central BP across obesity status.

This study adds to the literature new and more detailed findings regarding obesity and central BP relationships. In both youth and adults, central BP offers advantages with diagnosing and treating hypertension as well as being found as a better predictor of future CVD and events. However, further research is required before central BP can be clinically relevant in regards to CVD risk stratification and in the treatment of hypertension.

Table 1: Sample and Physical Characteristics of Participants

	Normal Weight	Overweight/ Obesity	Severe Obesity	
Covariates	**N = 120**	**N = 89**	**N = 99**	***P* value**
Age	12.5±2.5	12.5±2.5	13.0±2.8	0.31
Tanner				<0.01
1	48 (40.7%)	23 (26.7%)	16 (16.3%)	
2	20 (16.9%)	18 (20.9%)	26 (26.5%)	
3	17 (14.4%)	18 (20.9%)	18 (18.4%)	
4	22 (18.6%)	15 (17.4%)	22 (22.4%)	
5	11(9.3%)	12 (13.9%)	16 (16.3%)	
Sex				<0.01
Male	69 (58%)	43 (49.0%)	38 (38.4%)	
Female	50 (42.0%)	45 (51.0%)	61 (61.6%)	
Race				<0.01
White	108 (90.0%)	66 (74.2%)	67 (67.7%)	
African American	4 (3.33%)	8 (8.9%)	14 (14.1%)	
Other	8 (6.66%)	15 (16.9%)	18 (18.1%)	
Height (cm)	153.0 ± 15.0^{A}	156.3 ± 13.9^{B}	159.7 ± 12.5^{B}	<0.001
Weight (kg)	44.1 ± 13.1^{A}	65.9 ± 16.8^{B}	93.5 ± 26.7^{C}	<0.001
BMI (kg/m^2)	18.3 ± 2.4^{A}	26.5 ± 3.5^{B}	35.8 ± 6.1^{C}	<0.001
BMI Percentile	48.1 ± 22.4^{A}	95.4 ± 3.7^{B}	99.1 ± 0.5^{B}	<0.001
Waist Circumference (cm)	63.1 ± 6.9^{A}	80.5 ± 10.0^{B}	99.4 ± 14.0^{C}	<0.001
Heart Rate (bpm)	71 ± 15^{A}	75 ± 10^{B}	77 ± 11^{B}	<0.001

Data are mean±SD or n (%).
P value displayed is overall ANCOVA and post-hoc Tukey HSD - adjusted for age tanner stage, sex, and race.
Groups that do not share a letter are statistically different (*p<0.05)*
Abbreviations:.BMI - Body Mass Index.

Table 2: Body Composition

	Normal Weight	Overweight/ Obesity	Severe Obesity	
	N = 120	N = 89	N = 99	Overall P value
Total Body BMC (kg)	1.95±2.42	2.04±0.60	2.32±0.64	0.4
Total Lean (kg)	34.53±10.18 A	37.69±10.90 B	44.14±13.72 C	<0.001
Total Fat (kg)	16.32±4.05 A	24.62±8.38 B	37.10±14.08 C	<0.001
Body Fat (%)	25.1±6.1 A	39.5±7.2 B	48.0±4.9 C	<0.001
Visceral Fat Mass (kg)	0.07±0.54 A	0.41±0.28 B	1.09±0.58 C	<0.001
Android Lean (kg)	2.11±0.69 A	2.55±0.83 B	3.18±0.96 C	<0.001
Android Fat (kg)	0.48±0.32 A	1.88±0.90 B	3.95±1.62 C	<0.001
Gynoid Lean (kg)	5.19±1.79 A	5.73±1.97 B	7.29±4.12 C	<0.001
Gynoid Fat (kg)	2.76±0.83 A	4.03±1.52 B	6.22±3.29 C	<0.001

Groups that do not share a letter are statistically different (*p<0.001)*
Data are mean±SD or n (%).
P value is overall ANCOVA, post hoc Tuker HSD – adjusted for age, tanner stage, sex, and race.
Abbreviations: BMC – Bone Mineral Content

Table 3: Blood Pressure, Hemodynamics by Weight Status

	Normal Weight	Overweight/ Obesity	Severe Obesity	
	N = 120	N = 89	N = 99	Overall P value
Brachial				
SBP (mmHg)	105±10^{A}	113±11^{B}	122±12^{C}	<0.001
SBP Percentile (%)	44.0±24.9^{A}	63.0±26.5^{B}	78.5±23.4^{C}	<0.001
DBP (mmHg)	57±8^{A}	58±8^{A}	60±8^{B}	<0.001
DBP Percentile (%)	30.9±20.9^{A}	36.6±22.1^{AB}	42.8±22.8^{B}	<0.01
MAP (mmHg)	72±8^{A}	76±8^{B}	82±8^{C}	<0.001
Radial-Aorta				
r-a SBP (mmHg)	90±9^{A}	95±12^{B}	103±12^{C}	<0.001
r-a DBP (mmHg)	57±7^{A}	60±10^{A}	62±9^{B}	<0.001
r-a AiX (%)	1.0±12.9^{A}	3.0±14.7^{AB}	7.5±15.3^{B}	0.04
SBP (mmHg)	109±11^{A}	115±11^{B}	122±15^{C}	<0.001
Radial DBP (mmHg)	56±7^{A}	59±10^{AB}	61±9^{B}	<0.001
Carotid-Aorta				
c-a SBP (mmHg)	109± 12^{A}	114±13^{B}	122±15^{C}	<0.001
c-a DBP (mmHg)	57± 7^{A}	59±9^{AB}	61±8^{B}	<0.01
c-a AiX (%)	1.6± 18.7^{A}	-2.8±15.0^{B}	-4.8±15.3^{B}	0.04
Carotid SBP (mmHg)	116± 13^{A}	123±14^{B}	133±18^{C}	<0.001
Carotid SBP (mmHg)	57± 7^{A}	59±9^{AB}	60±8^{B}	0.02
Pulse Wave Velocity				
PWV R-C (m/s)	6.61±1.21	6.63±1.12	6.63±1.35	0.98

Groups that do not share a letter are statistically different (*p<0.001)*
Post-hoc Tukey HSD - adjusted for age, tanner stage, sex, and race.
Brachial SBP and DBP also adjusted for height.
Data are mean±SD or n (%). ANOVA – adjusted for age, tanner stage, sex, and race.

Table 4: BMI vs Blood Pressure Measures By Location

BMI	BP Variable	Overall r	Female r	Male r	p-value
	Brachial SBP				
	bSBP	0.64	0.55	0.72	<0.0001
	bSBP Percentile	0.49	0.46	0.49	<0.0001
	Brachial DBP				
	bDBP	0.39	0.39	0.38	<0.0001
	bDBP Percentile	0.23	0.27	0.17	<0.0001
	Central SBP				
	r-a SBP	0.57	0.44	0.67	<0.0001
	c-a SBP	0.52	0.41	0.66	<0.0001
	Central DBP				
	r-a DBP	0.41	0.36	0.43	<0.0001
	c-a DBP	0.39	0.35	0.41	<0.0001

Unadjusted Pearson Correlation. P-value represent overall r.
* represent p-value > 0.05
Abbreviations: BMI – body mass index; bSBP – brachial SBP;
bSBP% - bSBP percentile; bDBP – brachialDBP; bDBP% - bDBP percentile;
r-a SBP – radial aorta SBP; r-a DBP – radial aorta DBP;
c-a SBP – carotid aorta SBP; c-a DBP – carotid aorta DBP.

Table 5: BMI Percentile vs Blood Pressure Measures By Location

BMI Percentile	BP Variable	Overall r	Female r	Male r	p-value
	Brachial SBP				
	bSBP	0.49	0.43	0.56	<0.0001
	bSBP Percentile	0.49	0.46	0.49	<0.0001
	Brachial DBP				
	bDBP	0.28	0.27	0.27	<0.001
	bDBP Percentile	0.21	0.27	0.13	<0.01
	Central SBP				
	r-a SBP	0.33	0.25	0.37	<0.0001
	c-a SBP	0.31	0.22	0.41	<0.0001
	Central DBP				
	r-a DBP	0.23	0.2	0.24	<0.001
	c-a DBP	0.22	0.17	0.26	<0.01

Statistical Analysis: Unadjusted Pearson Correlation. P-value represent overall r.
* represent p-value > 0.05
Abbreviations: BMI – body mass index; bSBP – brachial SBP; bSBP% - bSBP percentile; bDBP – brachialDBP; bDBP% - bDBP percentile; r-a SBP – radial aorta SBP; r-a DBP – radial aorta DBP; c-a SBP – carotid aorta SBP; c-a DBP – carotid aorta DBP.

Table 6: Body Fat (%) vs Blood Pressure Measures By Location

Body Fat (%)	BP Variable	Overall r	Female r	Male r	p-value
	Brachial SBP				
	bSBP	0.49	0.42	0.56	<0.0001
	bSBP Percentile	0.56	0.48	0.58	<0.0001
	Brachial DBP				
	bDBP	0.31	0.29	0.29	<0.0001
	bDBP Percentile	0.26	0.29	0.23	<0.001
	Central SBP				
	r-a SBP	0.38	0.30	0.40	<0.0001
	c-a SBP	0.33	0.26	0.42	<0.01
	Central DBP				
	r-a DBP	0.24	0.19*	0.23	<0.001
	c-a DBP	0.19	0.20*	0.23	<0.01

Statistical Analysis: Unadjusted Pearson Correlation. P-value represent overall r.
* represent p-value > 0.05
Abbreviations: bSBP – brachial SBP; bSBP% - bSBP percentile; bDBP – brachialDBP; bDBP% - bDBP percentile; r-a SBP – radial aorta SBP; r-a DBP – radial aorta DBP; c-a SBP – carotid aorta SBP; c-a DBP – carotid aorta DBP.

Table 7: Visceral Fat Mass (kg) vs Blood Pressure Measures By Location

Visceral Fat Mass	BP Variable	Overall r	Female r	Male r	p-value
	Brachial SBP				
	bSBP	0.54	0.41	0.66	<0.0001
	bSBP Percentile	0.41	0.38	0.44	<0.0001
	Brachial DBP				
	bDBP	0.30	0.26	0.35	<0.0001
	bDBP Percentile	0.18	0.15*	0.22	<0.01
	Central SBP				
	r-a SBP	0.51	0.42	0.58	<0.0001
	c-a SBP	0.51	0.43	0.60	<0.0001
	Central DBP				
	r-a DBP	0.35	0.36	0.37	<0.0001
	c-a DBP	0.33	0.32	0.35	<0.0001

Statistical Analysis: Unadjusted Pearson Correlation. P-value represent overall r.
* represent p-value > 0.05
Abbreviations: bSBP – brachial SBP; bSBP% - bSBP percentile;
bDBP – brachialDBP; bDBP% - bDBP percentile; r-a SBP – radial aorta SBP;
r-a DBP – radial aorta DBP; c-a SBP – carotid aorta SBP; c-a DBP – carotid aorta DBP.

Table 8. Multiple linear regression analysis of Brachial BP Measurements

	β	SE	p-value	r^2, p-value
DV: Brachial SBP				
Age	0.2	0.4	0.58	
Tanner Stage	0.6	0.7	0.38	
Sex	1.2	1.3	0.33	
Race	-4.5	1.9	<0.01	
Height	0.3	0.07	<0.001	
[1]Body Fat (%)	0.5	0.05	<0.001	0.43, <0.001
[2]Viceral Fat Mass	0.009	0.001	<0.001	0.37, <0.001
DV: Brachial DBP				
Age	0.6	0.3	0.08	
Tanner Stage	0.02	0.5	0.98	
Sex	-0.9	1.0	0.37	
Race	-0.5	1.4	0.69	
Height	0.1	0.05	0.13	
[1]Body Fat (%)	0.2	0.05	<0.001	0.19, <0.001
[2]Viceral Fat Mass	0.003	0.001	<0.001	0.15, <0.001

Model [1] included Body Fat (%) and model [2] includes Visceral fat Mass (kg). Corresponding r^2 and p-value for each specific model are shown.

Table 9. Multiple linear regression analysis of Central BP Measurements

	β	SE	p-value	r^2, p-value
DV: Radial-Aorta SBP				
Age	1.6	0.4	<0.001	
Tanner Stage	1.0	0.8	0.18	
Sex	-1.1	1.5	0.48	
Race	-1.9	2.1	0.32	
[1]Body Fat (%)	0.42	0.07	<0.001	0.35, <0.001
[2]Viceral Fat Mass	0.008	0.001	<0.001	0.36, <0.001
DV: Radial-Aorta DBP				
Age	0.6	0.3	0.07	
Tanner Stage	1.2	0.6	0.06	
Sex	-1.4	1.2	0.26	
Race	-1.4	1.7	0.39	
[1]Body Fat (%)	0.2	0.05	<0.001	0.18, <0.001
[2]Viceral Fat Mass	0.004	0.001	<0.001	0.18, <0.001
DV: Carotid-Aorta SBP				
Age	1.6	0.5	<0.01	
Tanner Stage	1.5	1.0	0.13	
Sex	2.2	2.0	0.27	
Race	-3.7	2.9	0.15	
[1]Body Fat (%)	0.5	0.09	<0.001	0.30, <0.001
[2]Viceral Fat Mass	0.009	0.002	<0.001	0.31, <0.001
DV: Carotid-Aorta DBP				
Age	0.8	0.3	0.04	
Tanner Stage	1.2	0.6	0.03	
Sex	-0.1	1.3	0.46	
Race	-1.0	1.8	0.19	
[1]Body Fat (%)	0.1	0.05	<0.001	0.21, <0.001
[2]Viceral Fat Mass	0.003	0.001	<0.01	0.19, <0.001

Model [1] included Body Fat (%) and model [2] includes Visceral fat Mass (kg). Corresponding r^2 and p-value for each specific model are shown.

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