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Original Research

Carotid Artery IMT, Blood Pressure, and Cardiovascular Risk Factors in Males and Females

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ABSTRACT

International Journal of Exercise Science 9(4): 482-490, 2016. Previous studies have investigated carotid artery intima-media thickness (IMT) and blood pressure and found a direct correlation between the two. It is known that adult females have better cardiovascular health than males until a certain stage of life, yet limited research has examined gender differences in vascular function. Thus, the purpose of this study was to investigate vascular structure and function, blood pressure, and blood glucose/cholesterol levels in relation to gender differences in young healthy adults. On three separate days, 44 adults (26.30 ±11.9yrs; 24M, 20F) completed a carotid IMT ultrasound, a flow-mediated dilation (FMD), a fasted glucose and cholesterol test, a 24hr ambulatory blood pressure monitoring, a VO_{2max} test, and a body composition measurement. Females had lower systolic blood pressure, lower diastolic blood pressure, lower LDL/HDL ratios, lower body mass index, a higher HDL count, and lower plasma glucose levels than males ($p < 0.05$ for all), all of which suggest better cardiovascular health. However, we found no gender differences in vascular health measures, IMT and FMD. Our results suggest that while young adult females have better cardiovascular health than males, endothelial function may not yet be affected in the young adult years.

KEY WORDS: Blood pressure, intima-media thickness, cardiovascular, cholesterol, vascular health, glucose

INTRODUCTION

Cardiovascular (CV) disease is the leading cause of death in the world (4). Several CV disease risk factors include blood pressure, carotid artery intima-media thickness (IMT), flow-mediated dilation (FMD), volume of oxygen consumption (VO_{2max}), body composition, plasma fasted glucose, high density lipoprotein (HDL), low

density lipoprotein (LDL), and total cholesterol levels (15). Hypertension is defined as sustained elevation of brachial blood pressure and remains a common risk factor of CV disease (5, 17). Hypertension and CV disease are related to both vascular structure, measured by carotid artery IMT, and vascular function, assessed by FMD (14, 19). Research suggests that increased thickness of major arteries, such as the carotid artery, and impaired vascular function are early indicators of CV disease (21, 24). Separately, it has been shown that adults who were more physically active had better vascular health, and were therefore at a lower risk for CV disease (2, 26).

Increasingly, physicians are recommending ambulatory blood pressure (ABP) monitoring to assess hypertension in patients. ABP is a 24-hour home blood pressure monitoring system, which has been recommended for the identification of white coat hypertension, masked hypertension, nocturnal hypertension, well-controlled hypertension, and hypotension (3, 22). Finally, cholesterol levels are closely related to hypertension and CV disease. Previously, it has been shown that high LDL blood levels are associated with larger carotid IMT (18), and high HDL levels are associated with smaller carotid artery IMT measurements (29).

Hypertension is a serious risk factor of CV disease in both genders, and it has been proven that women with hypertension are more likely to have increased additional risk factors (increased total cholesterol, decreased LDL levels, and hyperglycemia) present compared to men (23). Women with hypertension were more likely to be older and have a higher BMI than men, which puts them at additional risk for a CV event (23). Also, research has shown that females have lower carotid IMT values, which suggests better CV health (16). In addition, throughout early adulthood in females, HDL levels are inversely related to carotid IMT measurements, but once women reach menopause the anti-atherogenic effects seem to diminish (11). Despite all of this, multiple studies have found that men are more likely to be hypertensive earlier in life (9, 28). One study found that hypertension is more prevalent in men until the sixth decade of life, which is when more women develop hypertension (28).

Despite the high number of cardiovascular studies conducted, limited research has examined gender differences in vascular function. Thus, the purpose of this study was to investigate vascular structure and function, blood pressure, and blood glucose/cholesterol levels in relation to gender differences in young healthy adults.

METHODS

Participants

Adult participants were recruited and asked to undergo a fasted test, a maximal graded exercise test, and wear a 24-hour ABP monitor, each of which occurred on three separate days. The fasted test consisted of FMD, carotid artery IMT, and a plasma glucose and cholesterol assessment. Only participants who completed these three portions of the study were included in this analysis. Data were collected and analyzed for 24 male participants and 20 female participants. Zero participants were excluded due to compliance reasons, although one participant was excluded due

to consumption of hypertension medication.

Specific criteria for inclusion were: non-diabetic, non-smoking, no medications that affect CV hemodynamics, no more than one anti-hypertensive medication, and no evidence or history of CV disease, hypercholesterolemia, or renal disease. Each participant gave written informed consent. The protocol was approved by the Ursinus College Institutional Review Board, and all procedures were in accordance with the ethical standards of the Helsinki Declaration.

Protocol

Office (clinic) blood pressure measurements were obtained in accordance with JNC-7 guidelines by laboratory personnel on three separate visits in a quiet (five minutes of rest), temperature controlled room (6), using an aneroid sphygmomanometer (Medline Industries, Model MDS9410, Mundelein, IL). Blood pressure measurements were performed in triplicate with the average of the three values used as the representative blood pressure for that visit. The mean systolic and diastolic blood pressure across the three visits is reported as the clinic blood pressure.

Twenty-four hour ABP monitoring was completed using a non-invasive portable blood pressure monitor (SpaceLabs, Model 90217, Redmond, WA), as previously described (8). Monitoring began in the morning of each participant's typical day. Blood pressure measures were obtained at 30-min intervals during the day (6:00am-10:00pm) and 60-min intervals at night (10:00pm-6:00am). The following morning, each participant was asked to list his or her waking hours to be used as the daytime blood pressure and sleep hours to be used as the nighttime blood pressure. Participant data were included in final analysis if more than 70% of the measurements were collected. Mean values were calculated for 24-hour average, daytime (awake), and nighttime (sleep) time frames.

Fasted plasma glucose and cholesterol levels were measured in participants using the Alere Cholestech LDX® lipid profile system (San Diego, CA). Blood was obtained by finger stick using a 35 µL lithium heparin-coated capillary tube, and tested immediately. Lipid profile test cassettes were inserted into the Cholestech system to analyze blood samples. Previously, finger stick Alere Cholestech LDX® lipid profile values were correlated ($r>0.95$) with venous plasma values measured in clinical diagnostic laboratories (Alere), which meets the National Cholesterol Education Program criteria for agreement between methods (10).

Participants were asked to refrain from food, exercise, medication, and caffeine for at least 10 hours prior to the test. The participant's height and weight were measured using a calibrated electronic scale without shoes. Body composition was measured in participants by whole-body bioelectrical impedance (BIA) using the single frequency impedance instrument (ImpediMed DF50, San Diego, CA) in a quiet, temperature-controlled room following an overnight fast. BIA was measured in accordance with the manufacturer's instructions at 50 kHz on the right side of the body. Two electrodes were placed on the dorsal right hand and foot while the participants were lying in a

supine position, and all electrode sites were cleaned with an alcohol swab before attachment. Three measurements were taken, and the mean values of impedance phase, resistance, and reactance were used for calculations of total fat mass and total fat free mass.

A maximal graded Bruce protocol exercise test was performed with continuous breath-by-breath gas sampling to measure oxygen consumption (VO_2) using a calibrated metabolic cart (TrueOne 2400, ParvoMedics, Sandy, UT). Electrocardiogram was continuously monitored by laboratory researchers (Nasiff CardioCard, Nasiff Associates, Central Square, NY). Blood pressure, heart rate, and perceived exertion were measured at each stage. The treadmill test was terminated using termination criteria according to American College of Sports Medicine Guidelines for Exercise Prescription and the American Heart Association (13).

Brachial artery diameter measurements using FMD were collected in a quiet room with no temperature variability, subsequent to a ten-hour overnight fast. Upon arrival, each participant was given a 20-minute resting time period for acclimation and to achieve a hemodynamic steady state. A 3-lead ECG was used to continuously measure heart rate. In addition, blood pressure was measured in the left arm to confirm a steady hemodynamic state. A 5x84-cm automatic cuff (E-20 rapid cuff inflator; D.E. Hokanson Bellevue, WA) was placed around the forearm just distal to the olecranon process, in accordance with current guidelines for obtaining FMD measures (7). Baseline images were obtained 2 to 10 cm superior to the antecubital fossa by 2D high resolution ultrasound system, using a 5 to 12 MHz multifrequency linear array transducer. Once a quality image was obtained, the right arm was supported, the position on patient arm marked, and the transducer was stabilized using a clamp. Minor corrections of transducer placement were made to maintain optimal imaging. Doppler velocity was also obtained through ultrasound imaging. Doppler flow signals were set at an insonation angle of 60°, and measurements were recorded with the sample volume placed along the middle of the artery. For 30 seconds, baseline measures were taken simultaneously with Doppler measurements for blood velocity and 2D ultrasound imaging for diameter. The automatic forearm cuff was then inflated to 250 mmHg and held at a constant pressure for 5 minutes. Diameter and velocity recordings resumed prior to cuff deflation and continued for 2 subsequent minutes as post-ischemia images were acquired. Ultrasound FMD videos were obtained with the GE Logiq E (Model BT12, GE Medical Systems, Chicago, IL), downloaded to a separate computer, and converted using Movavi Video Editor (Movavi, St Louis, MO). Arterial diameters were interpreted using the Brachial Analyzer for Research (Brachial Analyzer Version 6, Medical Imaging Applications, Coralville, IA). The highest 10 second interval throughout the 2 minute post-ischemic collection period represented the peak hyperemic diameter. Velocity and diameter measurements were converted to local shear stress using the following equation (20). Shear Stress = $8 \times \mu \times V_H/D_{BL}$, where μ is blood viscosity, assumed to be 0.035 dyne seconds/cm^2, V_H is the peak post-hyperemia velocity, and

D_{BL} represents the baseline diameter. FMD reported is the percent increase in diameter from baseline and is calculated as FMD = (peak hyperemic diameter – baseline diameter) / baseline diameter. The same operator performed all FMD measurements.

On the same day as FMD measurements, carotid artery IMT images were recorded and automatically calculated as previously described (12). Images were obtained and measurements made, for the right side common carotid artery, using the GE Logiq E ultrasound system and automated calculation software (Auto-IMT Software Option, GE Medical Systems, Chicago, IL). Three measures were collected of the posterior wall of the common carotid artery, as per established guidelines (25). The average of all the readings was calculated, and this value is reported. In our laboratory, the intraclass correlation coefficient for FMD is >0.84 and the ICC for average IMT is >0.94.

Statistical Analysis

Data are expressed as mean ± standard deviation (SD). Distribution of all variables was examined using the Shapiro-Wilk test of normality. Nonparametric tests were used when appropriate. Participants were split into two groups, males and females, for analysis. Independent t-tests were used to compare differences between males and females. Statistical significance was set a priori at $p < 0.05$. All statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Table 1 lists the participant characteristics. The sample of our study consisted of 44 participants (26.3 ± 11.9 yrs, 24 M, 20F). Average values for our whole sample group, male sample group, and female sample group can be found in Table 1.

Table 1. Participant Characteristics

	Whol	Male	Female	P-Value
Age, yrs	26.3 ±11.9	26.0 ±11.4	26.7 ±12.6	0.841
BMI, kg/m²	27.6 ±5.8	29.9 ±5.9	24.9 ±4.3	0.002
VO_{2max}, ml/kg/min	41.7 ±8.6	41.2 ±9.3	42.2 ±7.8	0.698
Systolic BP, mmHg	121.4 ±8.1	125.7 ±6.5	116.2 ±6.6	0.000
Diastolic BP, mmHg	75.0 ±5.5	76.9 ±4.5	72.7 ±5.8	0.012
Glucose	87.5 ±7.3	91.2 ±5.1	83.2 ±7.2	0.000
Cholesterol	164.2 ±36.7	164.6 ±38.2	163.9 ±36.0	0.958
Triglycerides	101.1 ±61.6	104.6 ±61.6	96.5 ±63.1	0.689
HDL	47.8 ±16.6	39.6 ±13.7	57.2 ±14.7	0.000
LDL	100.4 ±28.7	102.9 ±31.9	97.1 ±24.1	0.540
LDL/HDL	2.4 ±1.1	2.82 ± 1.2	1.73 ±0.62	0.001

Data are presented as mean ± standard deviation. BMI, body mass index; VO2max, maximum oxygen consumption; BP, blood pressure; HDL, high density lipoprotein; LDL, low density lipoprotein.

Significant differences were found between gender in several CV health measures. Male BMI was significantly greater than female BMI, as is shown in Table 1. Male systolic and diastolic blood pressure were also significantly higher than female blood pressure (Table 1). HDL cholesterol was significantly higher in females, and the LDL/HDL ratio was significantly higher in males (Table 1).

Table 2 lists vascular health measures by gender. In the entire group, a brachial artery baseline diameter and FMD of the brachial artery were measured and the results are presented in Table 2. Males had a significantly larger baseline diameter of the brachial artery.

Table 2. Vascular Health by Gender

	Males	Females	P-Value
Baseline Diameter	4.21 ± 0.64	3.48 ± 0.38	0.000
Flow Mediated Dilation	8.16 ± 3.8	6.86 ± 2.6	0.248
Intima-Media Thickness	0.50 ± 0.09	0.46 ± 0.06	0.095

Data are presented as mean ± SD.

For all forms of measurement, males had a significantly higher systolic blood pressure (See Figure 1).

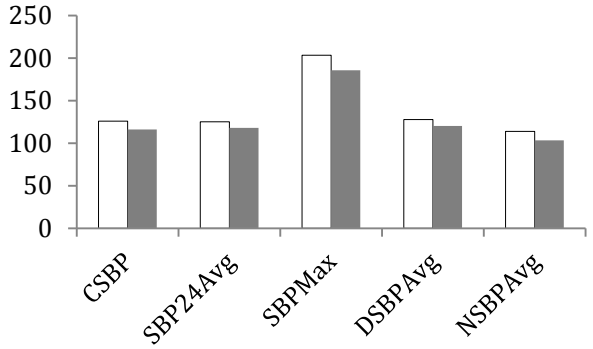

Figure 1. Systolic blood pressure differences between male and female adults. Values reported are means and in units of mmHg. White bars display male values and grey bars display female values. CSBP, clinic systolic blood pressure; SBP24Avg, ambulatory 24-hour systolic blood pressure average; SBPMax, maximum systolic blood pressure during exercise test; DSBPAvg, daytime 24-hour systolic blood pressure; NSBPAvg, night time 24-hour systolic blood pressure. *Significant p<0.05, between gender groups.

For the entire group, participants had an average body fat percentage of 31.3 ± 7.2 %. Participants had an average fat mass of 58.4 ± 25.2 lbs and an average fat free mass of 124.4 ± 13.3 lbs. When compared by gender, males were found to have a significantly higher BMI and fat free mass while females were found to have a significantly higher body fat percentage (See Figure 2).

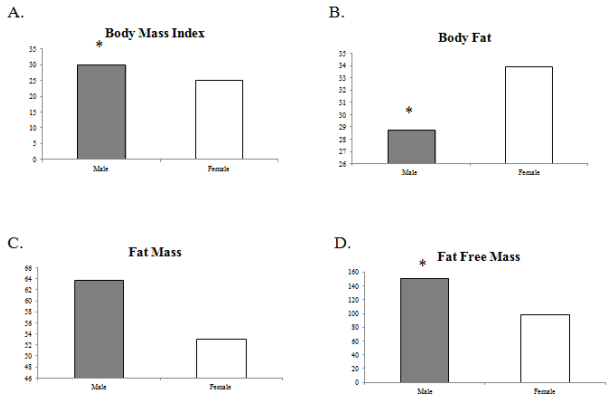

Figure 2. Differences in body composition in male and female adults. Grey bars display male values and white bars display female values. Values are means. *Significance p<0.05, between groups.

DISCUSSION

The main findings of this study are that young adult females have lower systolic blood pressure, lower diastolic blood pressure, lower LDL/HDL ratios, a higher HDL count, and lower fasting blood glucose levels than males, all of which are markers of increased CV health. However, we found no gender differences in vascular health measures, IMT and FMD. We also found that males have a significantly higher BMI than females, yet they also have significantly lower fat mass and significantly higher fat free mass than females. Our results suggest that while young adult females have better CV health than males, endothelial function may not yet be affected in the young adult years.

Gender differences in CV health are an extremely important topic and female CV health research is in high demand. Symptoms of CV disease present differently in males and females, therefore it is crucial to fully understand the gender differences among risk factors in order to improve prevention and detection of CV disease. It was found that men have significantly higher BP than females in all of our systolic blood pressure measurements (clinic blood pressure, 24 hour average, day time average, night time average, and max blood pressure). Several other studies have also concluded that males are more likely than females to have elevated blood pressure early in life (9, 28).

In our young sample (average age of 26.3 ± 11.9 yrs), it was found that females have healthier cholesterol levels than males. One study conducted by Appelman et al. examined gender differences in relation to CV disease and blood cholesterol levels (1). Researchers found that women of younger age have increased HDL and decreased LDL levels compared to males (1). Similar to their findings, we found that women have greater HDL levels and a lesser LDL/HDL ratio than males. Appelman et al. also found that after the menopausal transition, female LDL cholesterol levels become higher than males (1). As the female participants in our sample age, we suspect that, as a group, they will experience increased cardiovascular risk due to the loss of beneficial effects from female hormones.

In the current study, gender differences in vascular health measures were not observed. Since the other CV health measures were significantly different amongst genders, we inferred that IMT and FMD values had not yet been affected in our young and healthy population. A study conducted by Skaug et al. found that males had a higher prevalence of endothelial dysfunction than females (27). Skaug et al. also observed that the most marked reduction of FMD occurred in the early 30's in males and this reduction did not occur in females until their 40's. In both genders, the decline in endothelial function occurs approximately a decade prior to the largest increase in first CV event occurrence (27). In the current study, we did not see differences in endothelial function. We suspect this is because the average age of our sample was 26, and according to Skaug et al., FMD reduction does not commonly occur until the third and fourth decades of life. However, in our study we did find a significant difference in baseline diameter of the brachial artery. Even though vascular function is not different between genders, the difference in baseline diameter is expected because males are generally larger than females and subsequently have larger arteries. In addition, we found no gender differences in vascular structure, measured by carotid IMT.

There were several limitations to the current study. First, all participants were recruited from a suburban area. The sample recruited from this area may not be indicative of the general population. Also, the majority of our sample was comprised of college-aged young adults, which prevented us from observing the gender differences in CV health that are known to exist in older adults.

In conclusion, males and females experience differences in CV health due to

their gender. In our young sample, females have better CV health than males as evidenced by a lower blood pressure, higher HDL count, lower LDL/HDL ratio, and lower blood glucose levels. Vascular health has not yet been affected by gender in this young sample. Future research should investigate gender differences in CV health at different age ranges across the lifespan.

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