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The Influence of Gender on Carotid Artery Compliance and Distensibility in Children and Adults

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Abstract

Purpose—Given its association with the development of cardiovascular disease, compliance and distensibility measures of carotid arterial elasticity have been commonly used over the last decade as predictors of cardiovascular risk. However, the gender differences for these measures are unknown. The purpose of this study was to evaluate the impact of gender on carotid arterial elasticity in a large sample of children and adults.

Methods—Arterial elasticity measures of the carotid artery were obtained with ultrasound imaging in 294 children (157 males, 137 females; 6 to 18-yrs) and 604 adults (291 males, 311 females; 18–49 yrs) previously recruited for a study investigating cardiovascular risk factors. An independent sample t-test was used to compare demographic and carotid artery elasticity measures by age and gender.

Results—No significant gender differences in carotid arterial compliance and distensibility were observed in children. Adult females had significantly greater cross-sectional compliance compared to adult males (0.004±0.000 vs. 0.003±0.000 mm^2/mmHg, P=0.041).

Conclusions—A significant gender difference in carotid compliance was present in adults, but not in children. Thus, data from this study suggests that gender differences in arterial stiffness are not present early in life, but emerge later in adulthood.

Keywords

Ultrasound; Compliance; Distensibility; Youth; Adult

INTRODUCTION

Arterial elasticity has become an increasing focal point in the past decade because of its association with cardiovascular disease (CVD) [1,2]. The two most common measures of arterial elasticity are compliance and distensibility. By definition, compliance is the unit change in volume induced by a unit change in pressure, or the absolute change in arterial volume that reflects the arterial ability to store volume and reduce pressures [3,4], and distensibility is the relative change in arterial volume against the change in pressure and reflects the mechanical load placed on the arterial wall [4].

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Lower arterial compliance (i.e., the ability to expand and recoil), and/or increased arterial stiffness, is common with advancing age in both men and women [5,6]. Increased arterial stiffness is also associated with CVD risk factors, such as hypertension, hypertriglyceremia, type 2 diabetes mellitus, and aging [1,3,7–12]. Moreover, arterial stiffening impairs the ability of the arterial system to handle the spontaneous elevation in blood pressure at systole, which leads to increases in systolic blood pressure and left ventricular mass, as well as decreases in diastolic blood pressure and diastolic coronary perfusion [13].

Assessment of arterial compliance and distensibility within larger conduit arteries, such as the carotid artery, is a widely-used technique to examine vascular elasticity and arterial stiffness [14–22] given the abundance of elastic and collagen fibers within these arteries compared to smooth muscle fibers largely abundant in the peripheral vasculature. One may suspect there would exist a relationship between brachial and carotid arterial compliance and distensibility if arterial stiffness was systemically induced rather than occurring regionally.

The primary objective of this study was to evaluate the differences related to gender in carotid arterial elasticity measures in children and adults. We also examined, in a subset of participants, whether a relationship exists between brachial and carotid arterial elasticity measures. Gender differences relative to arterial stiffness, as well as potential arterial stiffness associations among different vascular beds, is critical to comprehensively understand the progression of atherosclerotic diseases and may showcase arterial differences with aging. We hypothesized that carotid artery elasticity will differ by gender and that differences will become more apparent with age (i.e., better identifiable in the adults compared to children). Additionally, we hypothesized that an association between brachial and carotid arterial elasticity may exist.

MATERIALS AND METHODS

The study protocol was approved by the University of Minnesota Institutional Review Board (IRB). The study procedures adhered to the University of Minnesota's IRB and the Health Insurance Portability and Accountability Act (HIPAA) guidelines. All subjects submitted written informed consent and assent for study participation.

Study Population

Eight hundred and ninety-eight subjects (448 males, 450 females) between the ages of 6 and 49-yrs (mean age 28.6±0.5 yrs; males: 28.1±0.7 yrs, females: 29.5±0.6 yrs) were included in the study. Subjects were recruited from a community-based sample and all subjects were healthy. These individuals were participants in a study investigating the early development of obesity, insulin resistance, and their interaction with associated cardiovascular risk factors. Subjects were stratified into 6 to 18-yrs and 18–49 yrs age group to separate the children from adults. Prior to vascular testing, subjects were asked to fast for 12-h and abstain from caffeine ingestion. Subjects were instructed to withhold morning medications until after vascular ultrasound testing, and refrain from strenuous physical activity 12-h prior to testing. A study physician and/or certified nurse practitioner was present to review study procedures and evaluation plans, prescription medications, and conduct comprehensive medical examinations including current and past medical history, review of systems (with particular attention to cardiovascular and endocrine issues), family history (with particular attention to cardiovascular disease and diabetes), and a physical examination.

All 898 subjects had carotid compliance and distensibility measures and a smaller subset of 93 individuals (55 males, 38 females) also had brachial artery measures. Data from this subset were further analyzed to determine if there is an association between brachial and carotid artery compliance and distensibility measures.

Measurements

Testing was performed in the Vascular Biology Laboratory in the University of Minnesota Clinical and Translational Science Institute. All the vascular studies were performed in a quiet, temperature-controlled environment (22–23°C).

Anthropometric and Blood Pressure Assessments—Measurements for height and weight were taken at the start of the visit using a digital stadiometer. Body Mass Index (BMI) was calculated as weight in kilograms (kg) divided by height in meters-squared (m^2). Seated blood pressure was obtained on the control arm using an automatic blood pressure monitor (Model BP-8800C; Colin Press-Mate, San Antonio, TX, USA).

Vascular Assessments—Brachial and carotid artery images, as well as supine systolic and diastolic blood pressure and pulse pressure, were concurrently measured by a non-invasive ultrasound with subjects in the supine position. Both brachial and carotid artery images were digitized and stored on a personal computer for later off-line analysis of arterial compliance and distensibility. Electronic wall-tracking software was used for the analysis (Vascular Research Tools 5, Medical Imaging Application, LLC, Iowa City, IA, USA).

Carotid artery measurements: Following 15-min of quiet rest in the supine position, vascular images were obtained of the carotid artery using the conventional ultrasound scanner (Acuson, Sequoia 512, Siemens Medical Solutions USA, Inc., Mountain View, CA, USA) with a 7.5 MHz linear array probe held at a constant distance from the skin and at a fixed point over the imaged artery. The transducer was held at a constant distance from the skin and at a fixed point over the common carotid artery, approximately 1-cm proximal from the carotid bifurcation bulb, to capture the left common carotid artery's lumen diastolic and systolic diameters. Images were collected at 20 frames per second for 10-s (200 frames) to ensure the capture of full arterial diameter change during a cardiac cycle. The mean diameter through the 10-s cycle was used to calculate measures of compliance and distensibility.

Brachial artery measurements: Following 15-min of quiet rest in the supine position, vascular images of the brachial artery in a smaller subset of 93 individuals were obtained using a conventional ultrasound scanner as previously described for carotid measurements. The transducer probe was held at a constant distance from the skin and the brachial artery was scanned in a fixed, longitudinal section 5 to 15-cm above the elbow with the assistance of a stereotactic arm. Depth and gain settings were set to optimize images taken of the lumen/arterial wall interface. The following procedures ensured consistency throughout subject analysis. Systolic and diastolic blood pressures were recorded with an automated blood pressure sphygmomanometer during both the 10-s carotid and brachial measurements. The ultrasound scanning system was interfaced with a standard personal computer equipped with a data acquisition card for attainment of radio frequency ultrasound signals from the scanner. Brachial artery image collection measurements were conducted similar to carotid artery measures.

Measurement Characteristics: In order to measure the brachial and carotid elasticity properties, the following formulas for distensibility and compliance were used:

- **Diameter distensibility** (DD, %) is defined as [(maxDiamM - minDiamM)/minDiamM]×100%.
- **Cross-sectional distensibility** (CSD, %) is defined as $[(\pi*(\text{maxDiamM}/2)^2 - \pi*(\text{minDiamM}/2)^2)/\pi*(\text{minDiamM}/2)^2] \times 100\%$.

- **Diameter compliance** (DC, mm/mmHg) is defined as [(maxDiamM - minDiamM)/ΔP].
- **Cross-sectional compliance 1** (CSC1, mm^2/mmHg) is defined as [(π*(maxDiamM/2)^2 - π*(minDiamM/2)^2)/(ΔP)].
- **Incremental elastic modulus** (IEM, mmHg) is defined as 3{1+[π*(maxDiamM/2)^2/ π*(minDiamM/2)^2}/CSC1.

Pulse pressure (ΔP) is calculated as the difference between systolic and diastolic pressures. Additionally, maxDiamM denotes maximum diameter measurement, and minDiamM denotes minimum diameter measurement. Furthermore, although multiple technicians were involved in the data collection, the software program utilized for vascular image assessment and interpretation was automated and operator-independent, minimizing any variability among technicians.

Statistical Analysis—Stata/SE 12.0 (StataCorp, College Station, TX, USA) was used for statistical analyses. Results are expressed as mean ± standard error of the mean (SEM). An independent sample t-test was used to compare demographic characteristics, as well as carotid artery compliance and distensibility measures by gender within the 6 to 18-yrs and 18–49 yrs age groups. A multiple linear regression model was additionally used to adjust for age, gender, and BMI or BMI Percentile where these risk factors were significantly different between genders in both age groups. Brachial versus carotid arterial compliance and distensibility measures were compared by Pearson's Correlation analysis within the smaller subset. An alpha value of 0.05 was used to signify statistical significance.

RESULTS

Carotid Artery Elasticity Assessment

Mean demographic data among both the male and female study population, stratified into two age groups (6 to 18-yrs, and 18–49 yrs) are presented in Table 1. For subjects 6 to 18-yrs of age, males were significantly taller (P=0.043), and had significantly higher seated systolic blood pressure (P<0.0001) and pulse pressure (P<0.0001) than females. Age (P=0.823), weight (P=0.309), BMI (P=0.895), BMI Percentile (P=0.957), and seated diastolic blood pressure (P=0.286) were not significantly different between males and females. For subjects 18–49 yrs of age, a significant difference in height (P<0.0001), weight (P<0.0001), as well as seated systolic blood pressure (P<0.0001), diastolic blood pressure (P=0.0001), and pulse pressure (P<0.0001) were reported between genders, with males reporting significantly higher values. Age (P=0.559) and BMI (P=0.270) were not significantly different between males and females.

Carotid artery measures of compliance and distensibility are displayed in Table 2. The letter 'c' is used to denote 'carotid' classifications when referencing all compliance and distensibility measures. Within the 6 to 18-yrs age group, females reported significantly greater supine diastolic blood pressure (P=0.033) compared to males, while males reported significantly greater supine pulse pressure (P=0.012) than females. No significant gender differences were reported among supine systolic blood pressure, diameter distensibility (cDD), cross-sectional distensibility (cCSD), diameter compliance (cDC), cross-sectional compliance 1 (cCSC1), and incremental elastic modulus (cIEM) measurements in children. Within the 18–49 yrs age group, males reported significantly greater supine diastolic blood pressure (P=0.0002) and supine pulse pressure (P=0.0001) compared to females, while females reported significantly greater cCSC1 (P=0.041) compared to males. Following adjustment for supine pulse pressure, cCSC1 was no longer significantly different between males and females (P=0.072). No significant gender differences were reported for cDD, cCSD, cDC, or cIEM measurements within the 18–49 yrs age group.

Additionally, adjustments for age, gender, and BMI Percentile in children or BMI in adults showed age was a significant negative predictor for adult cDD, cCSD, cDC, and cCSC1, yet was a significant positive predictor of cIEM for both children and adult age groups (P<0.05). BMI Percentile was a significant positive predictor of childhood cDD and cCSD, while BMI was a significant negative predictor of adult cDD, cCSD, cDC, and cCSC1 and a significant positive predictor of adult cIEM. Gender was not a significant predictor of any of the evaluated arterial elasticity measures.

Brachial and Carotid Artery Elasticity Assessment

A subset of 93 individuals was further analyzed to assess the relationship between brachial and carotid artery compliance and distensibility measures. Mean data for this subset are presented in Table 3. The letter 'b' is used to denote 'brachial classifications when referencing all compliance and distensibility measures. Among the 6 to 18-yrs age group, 39 subjects were available for analysis (22 males, 17 females). Among the 18–49 yrs age group, 54 subjects were available for analysis (33 males, 21 females). Age was not significantly different between males and females in the 6 to 18-yrs age group (12.0±0.7 vs. 12.5±0.8 yrs, P=0.639). Additionally, no significant differences among carotid or brachial measures of compliance and distensibility were reported within the 6–18 yrs age group. Within the 18–49 yrs age group, age was not significantly different between males and females (34.3±1.3 vs. 32.3±2.0 yrs, P=0.359). Adult males did report significantly larger cDD (P=0.004), cCSD (P=0.004), cCSC1 (P=0.026) compared to adult females, while adult females reported significantly higher cIEM (P=0.043) compared to adult males. There were no significant differences present among bDD, bCSD, cDC, bDC, bCSC1, and bIEM compliance and distensibility measures.

Brachial and Carotid Artery Elasticity Relationship—A significant correlation between brachial and carotid measures of compliance and distensibility was observed for DD (r=0.334, P=0.038), CSD (r=0.337, P=0.036), DC (r=0.367, P=0.025), and CSC1 (r=0.391, P=0.017) among the 6 to 18-yrs age group. No significant correlation between compliance and distensibility measures was observed for IEM (r=0.113, P=0.499). Among the 18–49 yrs subjects, a significant correlation between brachial and carotid measures of compliance and distensibility was observed for IEM (r=0.300, P=0.028). No significant correlation was observed between brachial and carotid measures of DD (r=0.191, P=0.166), CSD (r=0.190, P=0.168), DC (r=0.094, P=0.501), and CSC1 (r=0.243, P=0.090).

DISCUSSION

To our knowledge, this is the first study to evaluate the influence of gender on carotid arterial elasticity measures in a large sample of children and adults. Most arterial stiffness studies to date have been conducted in adult populations given arterial stiffness is common within the aging process of the arterial wall [23–25]. Furthermore, arterial stiffness is an important early marker of atherosclerotic disease identification. This is the first study, to our knowledge, to examine compliance and distensibility differences between genders in children.

The present study demonstrated that adult females had significantly greater carotid artery compliance compared to adult males, whereas in children compliance among males and females was not significantly different. Decreased arterial compliance has been shown to correlate with increased age [7,19,26–30], as well as gender and obesity [8,31–33]. Studies also have shown that sex hormones play an important role in vasomotion and vascular remodeling. Indeed, vascular function has been shown to change throughout the menstrual cycle [34]. Specifically, early luteal (EL) has been reported to significantly reduce flow-mediated dilation relative to early follicular (EF), late follicular (LF), and late luteal (LL) cycle stages, while whole body arterial compliance (WBAC) has been shown to significantly increase during the LF than in the EF and EL phases. Conversely, pulse wave velocity (PWV), a measure of regional compliance, did not vary over the four phases of the menstrual cycle [34]. Moreover, estradiol has been shown to promote nitric oxide (NO)-mediated vasodilatation, reduce vascular oxidative stress, and retard atherosclerosis [35–36]. Sherwood et al. [37] also reported that the effects of estrogen on receptors in vascular smooth muscle may be age-related; showing greater sensitivity in young, mature subjects as opposed to postmenopausal women. Furthermore, arterial stiffness and pulse pressure measures are often mitigated by sex steroids both pre- and post-puberty [38]. Therefore, the higher compliance of adult females compared to adult males may be due to the protective effects of estrogen.

The present study is also the first to examine the relationship between brachial and carotid arterial elasticity measures. A significant correlation between brachial and carotid measures of compliance and distensibility was observed for DD, CSD, DC, and CSC1 among the children. The adult group, on the other hand, displayed a significant correlation between brachial and carotid measures of IEM only. A clearer association between brachial and carotid measures of compliance and distensibility within the younger age group may also be specific to the effects of aging; further lending support to the negative relationship between aging and vessel compliance observed in the present study. Furthermore, it is possible that the high BMI values in adults, in relation to the children, may have explained some of the differences in arterial elasticity and vascular bed correlations. It is also possible that aging may play a roll in the mechanical changes in the vasculature.

Study strengths included the large sample size and wide age-range of the participants. A limitation of the study is that data on sexual development was not available in all children; therefore, a potential relation between pubertal development and differences in carotid artery compliance could not be assessed. Another limitation within this study is that physical activity level was not assessed. Studies suggest that increased physical activity improves arterial elasticity [41–42]; therefore, future studies assessing arterial elasticity in both children and adults should account for physical activity levels. Within the present study, participants were instructed to avoid strenuous exercise 24-h prior to vascular imaging to help minimize variability from such physical activity effects. And finally, vascular assessments were not timed around the menstrual cycle in females, which can be considered a limitation since cycle stage likely influences vascular function [34].

In summary, in this study of subjects between the ages of 6 and 49-yrs, adult females had significantly greater carotid artery compliance than adult males. No significant gender difference was observed within children suggesting that gender differences in arterial stiffness are not present early in life. A significant positive association also existed between brachial and carotid measures of DD, CSD, DC, and CSC1 group in the children, while a significant positive association between brachial and carotid IEM existed within the adult group. These findings suggest that arterial compliance and distensibility are somewhat similar among vascular beds during childhood but that differences emerge in adulthood. The clinical implications are not entirely clear; however, it is reasonable to speculate that arterial stiffening may occur earlier in certain vascular beds compared to others. Future research directed toward understanding the age at which arterial stiffening begins will have clinical and epidemiologic implications for early CVD prevention.

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Table 1

Mean (±SEM) Demographic Characteristics

	6 to 18-yrs		18–49 yrs	
	Male (n=157)	**Female (n=137)**	**Male (n=291)**	**Female (n=313)**
Age (yrs)	10.9±0.3	11.0±0.3	37.4±0.4	37.1±0.3
Height (cm)	149.8±1.6	145.3±1.5 *	178.5±0.4	164.6±0.4 *
Weight (kg)	48.8±2.0	46.0±1.9	91.5±1.1	79.4±1.3 *
BMI (kg/m^2)	20.5±0.5	20.6±0.5	28.6±0.3	29.3±0.5
BMI Percentile (%)	65.7±2.4	65.5±2.4	N/A	N/A
Seated SBP (mmHg)	105.2±0.8	100.4±0.8 *	119.1±0.7	109.9±0.8 *
Seated DBP (mmHg)	56.9±0.6	57.8±0.7	74.2±0.6	70.5±0.7 *
Seated PP (mmHg)	48.3±0.7	42.5±0.7 *	44.9±0.4	39.4±0.4 *

BMI, body mass index; Seated SBP, Seated systolic blood pressure; Seated DBP, Seated diastolic blood pressure; Seated PP, Seated pulse pressure;

* *P*-values <0.05 demonstrate significant differences between genders of the same age group (6 to 18-yrs, 18–49 yrs).

Table 2

Mean (±SEM) Carotid Artery Compliance and Distensibility Measures

	6 to 18-yrs			18–49 yrs		
	Male (n=157)	**Female (n=137)**	***P*-value**	**Male (n=291)**	**Female (n=313)**	***P*-value**
Supine SBP (mmHg)	109.7±1.0	108.9±1.1	0.598	126.6±0.8	121.9±1.0	0.0002
Supine DBP (mmHg)	55.2±0.7	57.3±0.7 *	0.033	72.9±0.6	69.5±0.6 *	0.0001
Supine PP (mmHg)	54.4±0.8	51.6±0.8 *	0.012	53.7±0.5	52.4±0.6 *	0.089
cDD (%)	15.2±0.3	14.9±0.3	0.536	8.3±0.2	8.4±0.1	0.542
cCSD (%)	32.9±0.7	32.3±0.8	0.536	17.3±0.3	17.5±0.3	0.533
cDC (mm/mmHg × 10^{-3})	15.8±0.5	15.8±0.4	0.963	10.6±0.2	10.4±0.3	0.587
cCSC1 (mm^2/mmHg × 10^{-3})	6.1±0.2	6.2±0.2	0.940	3.2±0.1	3.6±0.2 *	0.041
cIEM (mmHg)	963.7±42.6	918.7±26.6	0.386	1795.7±34.3	1760.7±49.5	0.566

Notation “c” denotes carotid artery measures; Supine SBP, supine systolic blood pressure; Supine DBP, supine diastolic blood pressure; Supine PP, supine pulse pressure; DD, diameter distensibility; CSD, cross-sectional distensibility; DC, diameter compliance; CSC1, cross-sectional compliance 1; IEM, incremental elastic modulus.

* *P*-values <0.05 denote significant differences between genders of the same age group (6 to 18-yrs, 18–49 yrs).

Table 3

Subset of Mean (±SEM) Brachial and Carotid Artery Compliance and Distensibility Measures

	6 to 18-yrs			18–49 yrs		
	Male (n=22)	**Female (n=17)**	***P*-value**	**Male (n=33)**	**Female (n=21)**	***P*-value**
cDD	15.0±0.6	15.3±0.8	0.756	11.0±0.6	8.5±0.4 *	0.004
bDD	3.0±0.2	2.6±0.3	0.320	2.5±0.2	2.7±0.3	0.572
cCSD	32.3±1.4	33.0±1.8	0.772	23.4±1.3	17.8±0.9 *	0.004
bCSD	6.1±0.4	5.4±0.6	0.323	5.1±0.4	5.5±0.6	0.562
cDC	16.2±0.1	17.6±0.1	0.262	13.1±0.7	11.4±0.7	0.089
bDC	2.2±0.3	2.7±0.1	0.628	1.8±0.1	2.3±0.4	0.104
cCSC1	6.0±0.3	6.5±0.3	0.215	4.3±0.3	3.5±0.2 *	0.026
bCSC1	1.4±0.3	2.2±0.1	0.423	1.4±0.3	1.7±0.3	0.792
cIEM	898.5±34.6	814.9±40.9	0.125	1,324.4±77.1	1,574.3±90.6 *	0.043
bIEM	5,617.5±429.1	6,170.9±866.2	0.544	6,838.3±502.3	6,091.5±515.9	0.326

Notation “b” denotes brachial artery measures and “c” denotes carotid artery measures; DD, diameter distensibility (%); CSD, cross-sectional distensibility (%); DC, diameter compliance, mm/mmHg × 10^{-3}; CSC1, cross-sectional compliance 1, mm^2/mmHg × 10^{-3}; IEM, incremental elastic modulus, mmHg.

* *P*-values <0.05 denote significant differences between brachial and carotid arterial measures of the same age group (6 to 18-yrs, 18–49 yrs).