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

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ABSTRACT: Purpose. Given the role of arterial wall elasticity in the development of cardiovascular disease, carotid artery compliance and distensibility have been used commonly over the last decade as predictors of cardiovascular risk, although their gender differences remain unknown. The purpose of our study was to evaluate the impact of gender on carotid arterial elasticity in a large sample of children and adults.

Methods. Carotid artery compliance and distensibility were measured with ultrasonography in 294 children (157 boys, 137 girls; ages 6–18 years) and 604 adults (291 men, 311 women; ages 18–49 years) previously recruited for a study investigating cardiovascular risk factors. An independent sample t test was used to compare demographic and carotid artery elasticity values by age and gender.

Results. No significant gender difference in carotid arterial compliance and distensibility was observed in children. Women had significantly greater cross-sectional compliance than men (0.004 ± 0.000 versus 0.003 ± 0.000 1/mmHg, p = 0.041).

Conclusions. We found significant gender difference in carotid compliance in adults, but not in children, suggesting that gender differences in arterial stiffness are not present early in life but emerge later in adulthood, © 2012 Wiley Periodicals, Inc. J Clin Ultrasound 41:340–346, 2013; Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/jcu.22015

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Decreased arterial elasticity has become a focal point in the past decade because of its association with cardiovascular disease (CVD).1,2 The two most common variables measuring arterial elasticity are compliance and distensibility. 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

Lower arterial compliance (ie, a decreased ability to expand and recoil) and increased arterial stiffness are common findings with advancing age in both men and women.5,6 Increased arterial stiffness is also associated with CVD risk factors, such as hypertension, hypertriglyceridemia, 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 an increase in systolic blood pressure and left ventricular afterload with a subsequent increase in myocardium mass, as well as a decrease in diastolic blood pressure and diastolic coronary perfusion.13

Assessment of arterial compliance and distensibility of large conduit arteries such as the carotid artery is a technique widely used to assess vascular elasticity and arterial stiffness,14–22 given the abundance of elastic and collagen fibers within the wall of these arteries, whereas smooth muscle fibers largely predominate in the peripheral vasculature. One may suspect a relationship

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between brachial and carotid arterial compliance and distensibility when cardiovascular disease induces systemic rather than regional arterial wall stiffness. The primary objective of this study was to evaluate the differences related to gender in carotid arterial elasticity in children and adults. We also investigated, in a subset of participants, the correlation between brachial and carotid arterial elasticity values. Gender-related differences in arterial stiffness, as well as the possibility of simultaneous and parallel involvement of different vascular beds in increased arterial wall stiffness, are critical to the comprehensive understanding of the progression of atherosclerotic diseases with aging. We hypothesized that carotid artery elasticity would differ by gender and that differences would become more significant with age (ie, more apparent in adults than in children). Additionally, we hypothesized an association between brachial and carotid arterial elasticity.

MATERIALS AND METHODS

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

Study Population

Eight hundred ninety-eight subjects (448 males, 450 females) between the ages of 6 and 49 years (mean age, 28.6 ± 0.5 years; males: 28.1 ± 0.7 years, females: 29.5 ± 0.6 years) 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-years and 18- to 49-years age groups to separate children from adults. Prior to vascular testing, subjects were asked to fast for 12 hours and abstain from caffeine ingestion. Subjects were instructed to withhold morning medications until after vascular ultrasound testing and refrain from strenuous physical activity 12 hours before testing. A study physician and/or a certified nurse practitioner were present to review the study procedures, and evaluation plans, and to 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 measurements, and a smaller subset of 93 individuals (55 males, 38 females) also had brachial artery measurements. Data from this subset were further analyzed to search for an association between brachial and carotid artery compliance and distensibility values.

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 of height and weight were taken at the start of the visit using a digital stadiometer and scale. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Seated blood pressure was obtained on the control arm using an automatic blood pressure monitor (Model BP-8800 C; Colin Press-Mate, San Antonio, TX).

Vascular Assessments

Brachial and carotid artery images, as well as supine systolic and diastolic blood pressure and pulse pressure, were measured concurrently by a noninvasive ultrasonographic system 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).

Carotid artery measurements. After 15 minutes of quiet rest in the supine position, vascular images of the carotid artery were obtained using a conventional ultrasound scanner (Acuson, Sequoia 512; Siemens Medical Solutions USA, Inc., Mountain View, CA) with a 7.5-MHz linear array probe. 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 seconds (200 frames) to ensure the capture of full arterial diameter change during a cardiac cycle. The mean diameter through the 10-second cycle was used to calculate compliance and distensibility.

Brachial artery measurements. After 15 minutes 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 5–15 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-second carotid and the 10-second brachial measurements. The ultrasound scanning system was interfaced with a standard personal computer equipped with a data acquisition card for acquisition of radiofrequency ultrasound signals from the scanner. Brachial artery image collection was conducted similar to carotid artery measures.

Measurement characteristics. To measure the brachial and carotid elasticity properties, the following formulas for distensibility and compliance were used:

- Diameter distensibility (DD, %) was calculated as $\frac{[D_{\text{max}} - D_{\text{min}}]/D_{\text{min}}] \times 100\%}.$
- Cross-sectional distensibility (CSD, %) was calculated as $\frac{[(\pi(0.5 D_{\text{max}})^2 - \pi (0.5 D_{\text{min}})^2)/\pi(0.5 D_{\text{min}})^2]} \times 100\%}.$
- Diameter compliance (DC, mm/mmHg) was calculated as $\frac{D_{\text{max}} - D_{\text{min}}}/\Delta P}.$
- Cross-sectional compliance (CSC, 1/mmHg) was calculated as $\frac{[(\pi(0.5 D_{\text{max}})^2 - \pi (0.5 D_{\text{min}})^2)/(\Delta P)]}.$
- Incremental elastic modulus (IEM, mmHg) was calculated as $3(1 + \frac{\pi(0.5 D_{\text{max}})^2}{\pi(0.5 D_{\text{min}})^2})/\text{CSC}.$

where $D_{\text{min}}$ is the minimum (diastolic) arterial lumen diameter, and $D_{\text{max}}$ is the maximum (systolic) arterial lumen diameter, and pulse pressure ($\Delta P$) is calculated as the difference between systolic and diastolic blood pressure. Furthermore, although multiple technicians were involved in the data collection, the software program used 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) was used for statistical analyses. Results are expressed as 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-years and 18- to 49-years age groups. A multiple linear regression model was additionally used to adjust for age, gender, and BMI or BMI percentile whenever these risk factors were significantly different between genders in both age groups. Brachial versus carotid arterial compliance and distensibility values 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 the female study population, stratified into two age groups (6–18 years and 18–49 years), are presented in Table 1. For subjects 6–18 years of age, boys were significantly taller ($p = 0.043$) and had significantly higher seated systolic blood pressure ($p < 0.0001$) and pulse pressure ($p < 0.0001$) than girls. 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 boys and girls. For subjects 18–49 years of age, males showed higher values than females 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 ($p < 0.0001$). Age ($p = 0.559$) and BMI ($p = 0.270$) were not significantly different between males and females.

Carotid artery values of compliance and distensibility are displayed in Table 2. The letter “c” is used to denote “carotid” when referencing compliance and distensibility values. Within the 6- to 18-years age group, girls had significantly greater
supine diastolic blood pressure \( p = 0.033 \) than boys, whereas boys had significantly greater supine pulse pressure \( p = 0.012 \). No significant gender differences were reported among supine systolic blood pressure, diameter distensibility \( \text{cDD} \), cross-sectional distensibility \( \text{cCSD} \), diameter compliance \( \text{cDC} \), cross-sectional compliance \( \text{cCSC} \), and incremental elastic modulus \( \text{cIEM} \) values in children. Within the 18- to 49-years age group, men had significantly greater supine diastolic blood pressure \( p = 0.0002 \) and supine pulse pressure \( p = 0.0001 \) than women, whereas women had significantly greater \( \text{cCSC} \) \( p = 0.041 \). After adjustment for supine pulse pressure, \( \text{cCSC} \) was no longer significantly different between men and women \( p = 0.072 \). No significant gender differences were reported for \( \text{cDD} \), \( \text{cCSD} \), \( \text{cDC} \), or \( \text{cIEM} \) within the 18- to 49-years age group.

Additionally, adjustments for age, gender, and BMI percentile in children or BMI in adults showed that age was a significant negative predictor for adult \( \text{cDD} \), \( \text{cCSD} \), \( \text{cDC} \), and \( \text{cCSC} \), yet was a significant positive predictor of \( \text{cIEM} \) for both children and adult age groups \( p < 0.05 \). BMI percentile was a significant positive predictor of childhood \( \text{cDD} \) and \( \text{cCSD} \), whereas BMI was a significant negative predictor of adult \( \text{cDD} \), \( \text{cCSD} \), \( \text{cDC} \), and \( \text{cCSC} \) and a significant positive predictor of adult \( \text{cIEM} \). Gender was not a significant predictor of any of the evaluated arterial elasticity variables.

### Brachial and Carotid Artery Elasticity Assessment

Mean data for the subset of subjects are presented in Table 3. The letter “b” is used to denote “brachial” when referencing compliance and distensibility values. Among the 6- to 18-years age group, 39 subjects were available for analysis (22 boys, 17 girls). Among the 18- to 49-years age group, 54 subjects were available for analysis (33 men, 21 women). Age was not significantly different between boys and girls in the 6- to 18-years age group (12.0 ± 0.7 versus 12.5 ± 0.8 years, \( p = 0.639 \)). Additionally, no significant differences among carotid or brachial compliance and distensibility were found within the 6- to 18-years age group. Within the 18- to 49-years age group, age was not significantly different between men and women (34.3 ± 1.3 versus 32.3 ± 2.0 years, \( p = 0.057 \)).
years, \( p = 0.359 \). Men did show significantly larger cDD (\( p = 0.004 \)), cCSD (\( p = 0.004 \)), or cCSC (\( p = 0.026 \)) than women, whereas women had significantly higher cIEM (\( p = 0.043 \)). There were no significant differences among bDD, bCSD, bDC, bDC, bCSC, and bIEM compliance and distensibility.

**Brachial and Carotid Artery Elasticity Relationship**

There was a significant correlation between brachial and carotid DD (\( r = 0.334, p = 0.038 \)), CSD (\( r = 0.337, p = 0.036 \)), DC (\( r = 0.367, p = 0.025 \)), and CSC (\( r = 0.391, p = 0.017 \)) among the 6- to 18-years age group, but not for IEM (\( r = 0.113, p = 0.499 \)). Among the 18- to 49-years subjects, there was a significant correlation between brachial and carotid IEM (\( r = 0.300, p = 0.028 \)), but not between brachial and carotid DD (\( r = 0.191, p = 0.166 \)), CSD (\( r = 0.190, p = 0.168 \)), DC (\( r = 0.094, p = 0.501 \)), and CSC (\( r = 0.243, p = 0.090 \)).

**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 because arterial wall stiffness is known to increase with age.21–25 Furthermore, arterial stiffness is an important early marker of atherosclerotic disease. Our study appears to be the first investigating compliance and distensibility differences between genders in children.

The present study demonstrated that women had significantly greater carotid artery compliance than men, whereas compliance was not significantly different between male and female children. Decreased arterial compliance has been shown to correlate with increased age7,19,26–30 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 cycle stage has been reported to reduce flow-mediated dilation significantly in comparison to early follicular, late follicular, and late luteal cycle stages, whereas whole body arterial compliance has been shown to be significantly greater during the late follicular than the early follicular and early luteal phases. Conversely, pulse wave velocity, 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–mediated vasodilatation, reduce vascular oxidative stress, and retard atherosclerosis.35,36 Sherwood et al37 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 values are often mitigated by sex steroids both pre- and postpuberty.38 Therefore, the higher compliance of women compared with men in our subjects 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. We found a significant correlation between brachial and carotid compliance and distensibility for DD, CSD, DC, and CSC among the children. The adult group, on the other hand, displayed a significant correlation.
between brachial and carotid 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, lending support to the negative relationship between aging and vessel compliance observed in the present study. Furthermore, the higher BMI values in the adults in comparison with the children may explain some of the differences in arterial elasticity and vascular bed correlations. It is also possible that aging may play a role in the mechanical changes in the vasculature.

Study strengths included the large sample size and a wide age range of the participants. A limitation of the study is that data on sexual development were not available in all children; therefore, a potential relation between pubertal development and differences in carotid artery compliance could not be assessed. Another limitation of this study is that physical activity level was not assessed. Studies suggest that increased physical activity improves arterial elasticity. 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 hours prior to vascular imaging to help minimize variability from such physical activity effects. Finally, vascular assessments were not timed around the menstrual cycle in women, which can be considered a limitation because cycle stage likely influences vascular function.

In summary, in this study of subjects between the ages of 6 and 49 years, women had significantly greater carotid artery compliance than men. 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 DD, CSD, DC, and CSC in the children, whereas 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 than in 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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