Childhood Blood Pressure as a Predictor of Arterial Stiffness in Young Adults
The Bogalusa Heart Study
Shengxu Li, Wei Chen, Sathanur R. Srinivasan, Gerald S. Berenson

Abstract—Increased arterial stiffness is an independent predictor of cardiovascular disease and mortality in middle-aged and older adults. However, limited data are available regarding the relationship of arterial stiffness in young adults with risk factors measured in childhood, adulthood, or as a cumulative burden from childhood to adulthood. This aspect was examined in a sample of 835 black and white young adults (72% whites, 44% men) aged 24 to 44 years who had at least 4 measurements of traditional risk factors over an average follow-up period of 26.5 years since childhood. Brachial-ankle pulse wave velocity (baPWV) measured by a simple automatic oscillometric technique was used as an index of arterial stiffness. The cumulative burden of risk factors since childhood was measured as area under the curve divided by follow-up years. In young adults, the baPWV was higher in males versus females (P<0.001) and blacks versus whites (P<0.001). In multiple regression analyses, independent predictors of baPWV in young adults were systolic blood pressure in childhood; systolic blood pressure, high-density lipoprotein cholesterol, triglycerides, and smoking in adulthood; and cumulative burden of systolic blood pressure and triglycerides and duration of smoking years from childhood. Thus, systolic blood pressure beginning in childhood is a consistent predictor of arterial stiffness in free-living, asymptomatic young adults. These findings underscore the importance of childhood blood pressure in the evolution of arterial stiffness and the need for beginning preventive cardiology early in life. (Hypertension. 2004; 43:541-546.)

Key Words: pulse wave velocity • cardiovascular disease • children • arteriosclerosis

Increased arterial stiffness, an independent predictor of cardiovascular (CV) disease risk and mortality, is associated with age, hypertension, end-stage renal disease, and atherosclerosis.1–5 Noninvasive devices such as Doppler ultrasound, MRI, or pulse wave velocity (PWV) measured by applanation tonometry6–9 are currently available to assess vascular stiffness. Of these, carotid–femoral PWV measured by applanation tonometry is widely being used. However, this methodology has certain limitations regarding the proper use of transducers. Recently, a simpler automatic oscillometric technique to measure brachial-ankle PWV (baPWV) has been developed,10,11 and its validity, reliability, and usefulness have been established and confirmed.10–15

It is well recognized that vascular changes including atherosclerosis begin early in life as a silent, asymptomatic disease process and are associated with CV risk factors.16,17 Importantly, CV risk factors persist or track from childhood to adulthood and are predictive of CV disease risk in adults.18,19 Evaluation of arterial stiffness and its predictors may help identify asymptomatic individuals at risk. In this regard, no data are available with respect to whether and what extent childhood traditional CV risk factors and their cumulative burden from childhood to adulthood are associated with arterial stiffness measured in young adulthood. Longitudinal data from the Bogalusa Heart Study, a biracial (black–white) community-based investigation of CV risk factors beginning in childhood,20 provide an opportunity to explore the importance of traditional CV risk factors measured in childhood, adulthood, or as a cumulative burden from childhood to adulthood in influencing arterial stiffness.

Methods

Population
Between 1973 and 2001, seven cross-sectional surveys of children aged 4 to 17 years and 7 surveys of young adults aged 18 to 44 years who participated earlier as children and remained accessible were conducted in the biracial (65% whites, 35% blacks) community of Bogalusa, Louisiana. This panel design, based on repeated cross-sectional examinations conducted approximately every 3 to 4 years, resulted in multiple observations during childhood and young adulthood. These observations enabled an evaluation of the cumulative burden of each risk factor beginning in childhood. From the most recent 2000-2001 survey of young adults, baPWV measurements were obtained for 835 (aged 24 to 44 years, mean age 36.0 years; 72% white, 45% men) participants. These subjects were previously examined 4 or more...
times (at least once in childhood, one time in adulthood: 76% had at least 6 measurements). The average follow-up period was 26.5 years (range: 16.9 to 29.6 years). Participation rates ranged from approximately 80% to 92% for school-aged children to approximately 60% to 65% for the adult cohort. Written informed consent was obtained from parents or guardians in childhood and from the participants in adulthood. Protocols were approved by the Institutional Review Board of the Tulane University Health Sciences Center.

Examinations
All surveys followed essentially the same protocol for risk factor measurements.28 Participants were instructed to fast for 12 hours before screening, with compliance ascertained by interview on the morning of the examination. Height and weight were measured twice to within 0.1 cm and within 0.1 kg, respectively, and the mean values were used to calculate body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters) as a measure of body fatness. Information on smoking status (yes/no) was obtained as part of a health habit questionnaire,21 and duration (years) of smoking was obtained in adulthood in the last 2000-2001 survey.

Replicate blood pressure measurements were obtained on the right arm of the participants in a relaxed, sitting position. Arm measurements, length and circumference, were made during the examination to ensure proper cuff size. Systolic and diastolic blood pressure levels were analyzed as the first, fourth (in children), and fifth (in adults) Korotkoff phases using mercury sphygmomanometers. Blood pressure levels were reported as the mean of 6 replicate readings, taken by each of 2 randomly assigned and trained observers.

Serum Lipid and Lipoprotein Analyses
During 1973 to 1986, cholesterol and triglycerides levels were measured with a Technicon AutoAnalyzer II (Technicon Instrument Corp, Tarrytown, NY) according to the Laboratory Manual of the Lipid Research Clinics Program.22 These variables were determined by enzymatic procedures23,24 on the Abbott VP instrument (Abbott Laboratories, North Chicago, Ill) between 1986 and 1996 and on the Hitachi 902 Automatic Analyzer (Roche Diagnostics, Indianapolis, Ind) since then. Both chemical and enzymatic procedures met the performance requirements of the Lipid Standardization Program of the Centers for Disease Control and Prevention (CDC). This standardization monitored the accuracy of measurements of total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol concentrations. Measurements on CDC-assigned quality-control samples showed no consistent bias over time within or between surveys. Serum lipoprotein cholesterol levels were analyzed using a combination of heparin–calcium precipitation and agar–agarose gel electrophoresis procedures.25

Pulse Wave Velocity Measurements
baPWV was measured using a noninvasive automatic oscillometric device (BP-203RPE; Colin, Komaki, Japan) as described in detail previously.10,11 This instrument records PWV, blood pressure, ECG, and heart sounds simultaneously. Occlusion and monitoring cuffs were placed snugly around both sides of the upper and lower extremities in subjects in the supine position. After at least 5 minutes of bedrest, 3 waveforms of brachial and tibial arteries were recorded. ECG monitoring was performed with electrodes placed on both wrists. The pressure waveforms obtained at the 2 different sites were simultaneously recorded to examine the time interval between the initial rise in the brachial and tibial pressure waveforms (Ta). The path length from the suprasternal notch to the elbow (Da) and the path length from the suprasternal notch to the ankle (Db) were obtained automatically based on the subject’s height. Finally, baPWV was calculated with the equation: (Db−Da)/Ta. To examine the reproducibility of baPWV, 37 randomly selected subjects were reexamined 2 to 3 hours later, after their first examination. The correlation coefficient between 2 examinations was 0.84 for the left side (P<0.001) and 0.82 for the right side (P<0.001). The average value of measurements on both left and right sides was used for data analysis.

Statistical Methods
All data analyses were performed using SAS version 8. The area under the curve (AUC) of serial measurements was used as a measure of cumulative risk burden from childhood to adulthood and its computation has been described previously in detail.26 Age was centered by subtracting 20, which was the average value of age in the total sample.

Risk factors measured at the first and last examinations were used as childhood and adulthood values, respectively. Pearson correlation coefficients were used to assess the relationships of baPWV to risk factors measured since childhood, with childhood and adult risk factors standardized to race-, sex-, and age-specific z scores; AUC values to race-, sex-, and average age-specific z scores; and baPWV to race-, sex-, age-, and heart rate-specific z scores. Adjustment of baPWV for heart rate was necessary because it is an important confounder of PWV.27,28 To explore the predictors of baPWV in young adults, multiple regression analysis was performed with baPWV as a dependent variable and risk factors measured since childhood as the independent variables, respectively, with all the variables standardized as described.

Results
Mean values of risk factor variables and their cumulative burden from childhood to adulthood in the study cohort are shown in Table 1 by race and sex. With some exceptions in particular race, sex, and age groups, blacks versus whites in general had higher systolic blood pressure and HDL cholesterol and lower triglycerides; males versus females had higher systolic blood pressure, low-density lipoprotein (LDL) cholesterol, triglycerides, and lower HDL cholesterol; white men and black women had higher BMI than white women and black men, respectively.

Mean levels along with certain percentiles of baPWV in young adults by race and sex are shown in Table 2. Blacks versus whites and men versus women had higher baPWV (P<0.001). Pearson correlation coefficients between baPWV in young adulthood and risk factor variables measured from childhood to adulthood are shown in Table 3. Childhood systolic blood pressure, BMI, and HDL cholesterol (inverse association) were significantly correlated with baPWV in young adults. In adulthood, systolic blood pressure, triglycerides, BMI, HDL cholesterol (inverse association), and LDL cholesterol were all significantly correlated with baPWV, with systolic blood pressure showing the highest correlation. For risk factors measured as a cumulative burden since childhood, all risk factors were significantly correlated with baPWV in young adults, and the magnitude of correlation was highest for systolic blood pressure.

Table 4 shows results of multiple regression of baPWV on risk factor variables measured since childhood. Childhood systolic blood pressure was the only independent predictor for baPWV in young adults. In adulthood, systolic blood pressure, smoking, HDL cholesterol (inverse association), and triglycerides were independent correlates of baPWV. Cumulative burdens of systolic blood pressure, smoking (duration), and triglycerides since childhood were independent predictors of baPWV in
TABLE 1. Mean±SD Levels of Risk Factor Variables and Their Cumulative Burden From Childhood to Adulthood in the Study Cohort by Race and Sex

<table>
<thead>
<tr>
<th></th>
<th>White (Male n=284)</th>
<th>Female (n=320)</th>
<th>Black (Male n=90)</th>
<th>Female (n=141)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Childhood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>9.7±3.2</td>
<td>9.5±3.3</td>
<td>9.7±3.0</td>
<td>9.3±3.0</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>17.5±3.1</td>
<td>17.5±3.3</td>
<td>17.0±2.6</td>
<td>17.1±3.4</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>100.1±9.6</td>
<td>99.0±9.7</td>
<td>99.0±11.4</td>
<td>97.5±10.0</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>65.7±22.1</td>
<td>61.6±21.4</td>
<td>68.2±20.6</td>
<td>71.5±19.6</td>
<td>&lt;0.001* &lt;0.05†</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>88.6±26.0</td>
<td>92.8±25.5</td>
<td>90.6±26.6</td>
<td>92.2±23.6</td>
<td>NS    &lt;0.05†</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>66.1±35.7</td>
<td>76.6±34.8</td>
<td>59.0±27.9</td>
<td>60.1±20.6</td>
<td>&lt;0.001* &lt;0.001†</td>
</tr>
<tr>
<td><strong>Adulthood</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>36.4±4.4</td>
<td>36.1±4.6</td>
<td>36.4±4.7</td>
<td>35.2±5.2</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.0±5.8</td>
<td>28.3±6.9</td>
<td>29.1±6.4</td>
<td>31.4±8.4</td>
<td>&lt;0.001* &lt;0.05‡</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>117.7±11.2</td>
<td>110.3±11.4</td>
<td>127.7±15.7</td>
<td>117.5±14.1</td>
<td>&lt;0.001 &lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>40.3±9.6</td>
<td>48.9±11.4</td>
<td>46.5±13.1</td>
<td>50.6±12.3</td>
<td>&lt;0.01 &lt;0.001</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>129.1±33.6</td>
<td>124.2±32.0</td>
<td>127.8±47.8</td>
<td>114.3±31.2</td>
<td>&lt;0.001* &lt;0.001‡</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>164.1±135.9</td>
<td>125.0±76.3</td>
<td>139.6±119.4</td>
<td>87.4±38.4</td>
<td>&lt;0.05 &lt;0.001</td>
</tr>
<tr>
<td><strong>Cumulative burden (AUC)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average age (y)</td>
<td>20.1±4.1</td>
<td>20.2±3.9</td>
<td>19.8±3.8</td>
<td>19.5±3.8</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.6±4.5</td>
<td>23.5±4.6</td>
<td>23.9±4.1</td>
<td>25.3±5.4</td>
<td>NS    &lt;0.05</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>111.1±6.6</td>
<td>107.0±6.2</td>
<td>113.6±6.4</td>
<td>109.4±6.3</td>
<td>&lt;0.01 &lt;0.001</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>46.7±8.5</td>
<td>52.5±7.7</td>
<td>55.3±10.4</td>
<td>56.6±8.1</td>
<td>&lt;0.001 &lt;0.001‡</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>103.7±22.1</td>
<td>103.7±20.6</td>
<td>101.2±26.5</td>
<td>102.7±23.1</td>
<td>NS</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>94.2±39.2</td>
<td>89.6±25.6</td>
<td>76.6±32.3</td>
<td>70.0±14.7</td>
<td>&lt;0.001 NS</td>
</tr>
</tbody>
</table>

P values were adjusted for covariates when appropriate. AUC indicates area under the curve divided by follow-up years; BMI, body mass index; BP, blood pressure; TG, triglycerides.
*Only in females.
†Only in whites.
‡NS indicates there was no significant difference between groups.

TABLE 2. Mean (±SD) and Selected Percentiles of Brachial-Ankle Pulse Wave Velocity by Race and Sex

<table>
<thead>
<tr>
<th></th>
<th>Mean (±SD) (cm/s)</th>
<th>Percentile (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5th</td>
<td>10th</td>
</tr>
<tr>
<td>White men</td>
<td>1377±163</td>
<td>1133</td>
</tr>
<tr>
<td>White women</td>
<td>1239±182</td>
<td>944</td>
</tr>
<tr>
<td>Black men</td>
<td>1478±207</td>
<td>1198</td>
</tr>
<tr>
<td>Black women</td>
<td>1289±225</td>
<td>943</td>
</tr>
</tbody>
</table>

P<0.001 for comparison of means between blacks and whites and between men and women, adjusted for age, heart rate, and sex/race.

Discussion

The present study demonstrates that blacks versus whites and men versus women have increased vascular stiffness measured as baPWV. Systolic blood pressure in childhood, systolic blood pressure, smoking, HDL cholesterol (inverse association), triglycerides in adulthood, and cumulative burden of systolic blood pressure, smoking, and triglycerides since childhood are independent predictors of baPWV in adulthood. Of note, systolic blood pressure measured since childhood was a consistent and independent predictor of baPWV in adults. These observations from a community-based cohort free from the selection bias of a patient population indicate that systolic variations of arterial stiffness can be assessed in asymptomatic, healthy young adults by a simpler oscillometric device and that childhood systolic blood pressure plays an important role in the process of arterial stiffening.

In this study, one single measurement of systolic blood pressure in childhood, regardless of its minute-to-minute variation, was associated with baPWV in young adults. Those who had higher blood pressure levels in childhood had stiffer arteries 26 years later, which suggests that blood pressure even in early childhood plays a role in the process of arterial stiffening. This is consistent with earlier reports showing an inverse association between arterial elasticity or compliance and blood pressure in youth. Mechanistically, arterial stiffness may be the consequence of repetitive cycles of stress and strain and the attendant induction of vascular smooth muscle cell growth and synthesis of matrix components. Smooth muscle cell phenotype and activity modulate the proportion of elastin to collagen, thereby influencing vascular stiffness, which...
may further increase blood pressure and start a vicious cycle.

The observed predictability of childhood blood pressure for arterial stiffness in young adulthood is at variance with the situation in middle-aged and older adults in whom impaired elasticity or compliance of the artery is considered an antecedent factor for systolic hypertension and widened pulse pressure. It should be noted that the early phase of high blood pressure seen in youth is generally governed by increases in sympathetic nervous system activity and peripheral vascular resistance resulting in arterial stiffness, whereas the manifestation of later-phase hypertension in the elderly is influenced more by increases in central vessel stiffness than sympathetic activity.

Recently, others and we have shown that childhood risk factors are predictive of carotid vascular changes measured in terms of carotid intima-medial thickness in young adults. Although atherosclerosis involves complex mechanisms including fat deposition (atherosis) and medial degeneration (sclerosis), arterial wall thickening or atherosis results mainly from risk factors such as dyslipidemia. In general, elevated arterial PWV is a measure of sclerosis, which is mainly caused by aging, and elastic fiber degeneration related to long-term repetitive stress/strain burden of hemodynamic forces. Given that both arterial stiffness and thickness are important markers of future CV risk, the current study along with previous studies again underscores the importance of childhood risk factors in the development of CV risk in adulthood.

The present study, as in previous studies, shows that systolic blood pressure along with HDL cholesterol (inverse association), triglycerides, and smoking in adulthood are cross-sectionally associated with baPWV in young adulthood. Similar trends were also seen in the current study with respect to cumulative burden of these variables (except for HDL cholesterol). Further, insulin resistance status measured cross-sectionally in adulthood by fasting glucose and insulin was also an independent determinant of arterial stiffness. Unfortunately, those measurements were not available in childhood in this cohort. Thus the influences of insulin resistance in childhood or as a cumulative burden on arterial stiffness in young adults could not be examined in this study. Taken together, these data indicate hemodynamics of the circulation system and metabolic factors are aspects determining arterial stiffness.

**Perspectives**

The results in this study show that systolic blood pressure measured in childhood, adulthood, or as a cumulative burden are cross-sectionally associated with baPWV in young adulthood. Similar trends were also seen in the current study with respect to cumulative burden of these variables (except for HDL cholesterol). Further, insulin resistance status measured cross-sectionally in adulthood by fasting glucose and insulin was also an independent determinant of arterial stiffness. Unfortunately, those measurements were not available in childhood in this cohort. Thus the influences of insulin resistance in childhood or as a cumulative burden on arterial stiffness in young adults could not be examined in this study. Taken together, these data indicate hemodynamics of the circulation system and metabolic factors are 2 aspects determining arterial stiffness.

**TABLE 3. Pearson Correlation Coefficients Between Brachial-Ankle Pulse Wave Velocity in Young Adulthood and Risk Factor Variables Measured From Childhood to Adulthood**

<table>
<thead>
<tr>
<th></th>
<th>BMI</th>
<th>Systolic Blood Pressure</th>
<th>HDL Cholesterol</th>
<th>LDL Cholesterol</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood (4 to 17 years)</td>
<td>0.091†</td>
<td>0.111†</td>
<td>−0.075*</td>
<td>0.029</td>
<td>0.062</td>
</tr>
<tr>
<td>Adulthood (24 to 44 years)</td>
<td>0.153‡</td>
<td>0.471‡</td>
<td>−0.147‡</td>
<td>0.100†</td>
<td>0.190‡</td>
</tr>
<tr>
<td>Cumulative burden (AUC)</td>
<td>0.150†</td>
<td>0.319‡</td>
<td>−0.086*</td>
<td>0.082*</td>
<td>0.162‡</td>
</tr>
</tbody>
</table>

AUC indicates area under the curve divided by follow-up years. Race-, sex-, and age-specific z scores were used for risk factor variables. Race-, sex-, age-, and heart rate-specific z scores were used for baPWV.

*P<0.05; †P<0.01; ‡P<0.001.

**TABLE 4. Multiple Regression of Brachial-Ankle Pulse Wave Velocity in Young Adults on Risk Factor Variables Measured Since Childhood**

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Childhood</th>
<th>Adulthood</th>
<th>Cumulative Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>P</td>
<td>β</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>β</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>β</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.085</td>
<td>0.021</td>
<td>0.436</td>
</tr>
<tr>
<td>BMI</td>
<td>0.041</td>
<td>0.268</td>
<td>−0.060</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>−0.050</td>
<td>0.150</td>
<td>−0.071</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.0003</td>
<td>0.992</td>
<td>0.027</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.015</td>
<td>0.714</td>
<td>0.005</td>
</tr>
<tr>
<td>Smoking*</td>
<td>0.027</td>
<td>0.936</td>
<td>0.145</td>
</tr>
</tbody>
</table>

AUC indicates area under the curve divided by follow-up years; BMI, body mass index. Race-, sex-, and age-specific z scores were used for risk factor variables. Race-, sex-, age-, and heart rate-specific z scores were used for baPWV.

*Childhood and adulthood: no=0, yes=1; cumulative burden: duration of smoking (years).
burden since childhood is a consistent predictor of arterial stiffness in young adults. This underscores the importance of systolic blood pressure in the evolution of arterial stiffness. Further, HDL cholesterol and triglycerides as independent correlates for arterial stiffness reflect the role of metabolic factors in addition to hemodynamic stress in the arterial stiffening. Although the causality between childhood blood pressure and arterial stiffness in young adults could not be established by this observational study, information from our study and other accumulating evidence showing that childhood risk factors are predictive of CV risk later in life underscore the relevance of preventive cardiology early in life.

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