Correlates of Common Carotid Artery Lumen Diameter in Black and White Younger Adults
The Bogalusa Heart Study

Litao Ruan, MD, PhD; Wei Chen, MD, PhD; Sathanur R. Srinivasan, PhD; Meihung Sun, MPH; Hongwei Wang, MS; Ahmet Toprak, MD; Gerald S. Berenson, MD

Background and Purpose—Vascular remodeling as depicted by increases in arterial lumen diameter occurs in response to development of atherosclerosis. However, data on the correlates of arterial lumen diameter in younger adults by race and sex are limited.

Methods—The study cohort included 734 white and 306 black subjects, aged 20 to 43 years, enrolled in the Bogalusa Heart Study. The common carotid artery lumen diameter at diastole and intima media thickness (IMT) were measured by M- and B-mode ultrasonography, respectively.

Results—As a group, blacks versus whites (3.44 mm/m versus 3.37 mm/m, \( P = 0.002 \)) and males versus females (3.45 mm/m versus 3.35 mm/m, \( P < 0.001 \)) had greater height-adjusted lumen diameter. In multivariate analyses of total sample, body mass index, mean arterial pressure, heart rate, and carotid IMT were independent predictors of height-adjusted lumen diameter. The magnitude of the effects of mean arterial pressure and carotid IMT on height-adjusted lumen diameter was significantly different between races with blacks showing greater slopes (difference in slopes: \( P = 0.011 \) for mean arterial pressure; \( P = 0.033 \) for IMT); interaction effects of body mass index and mean arterial pressure with sex on height-adjusted lumen diameter were also noted with males showing steeper slopes (difference in slopes: \( P = 0.003 \) for body mass index; \( P = 0.005 \) for mean arterial pressure). In addition, the lumen diameter–carotid IMT relationship was stronger in hypertensives than in normotensives (difference in slopes: \( P = 0.038 \)).

Conclusions—Common carotid artery lumen diameter is influenced by carotid artery IMT, adiposity, and blood pressure in a race- and sex-specific manner in asymptomatic younger adults, which may have implications for preventive cardiology. (Stroke. 2009;40:702-707.)

Key Words: cardiovascular risk factors ▪ carotid artery ▪ intima media thickness ▪ lumen diameter ▪ younger adults

As originally proposed by Glagov et al,1 studies have shown that development of atherosclerosis can result not only in arterial wall thickening, but also in adaptive response of the arterial wall to disease process, known as compensatory lumen enlargement.2–4 The vascular remodeling is considered a compensation for initiation of atherosclerosis to preserve lumen diameter and restore normal blood flow. Arterial diameter is known to be influenced by arterial wall thickness as well as age, race, sex, and anthropometric, metabolic, and hemodynamic parameters.5–11 However, most of the previous findings in this regard were based on patients and middle-aged and older adults. As part of the Bogalusa Heart Study, a biracial (black–white) community-based epidemiological study of the early natural history of cardiovascular (CV) disease,12 the present study examined the cross-sectional relationships of traditional CV risk factor variables and carotid artery intima media thickness (IMT) to common carotid artery lumen diameter in asymptomatic younger adults by race and sex.

Methods

Study Cohort
A total of 1073 subjects aged 20 to 43 years (mean age, 35.6±4.6 years) were examined in 2001 to 2002 for CV risk factors and carotid artery IMT and lumen diameter. Exclusion of subjects (n=33) who had nonfasting blood samples resulted in 1040 subjects (734 whites and 306 blacks) for this analysis. All subjects in this study gave informed consent at examination. Study protocols were approved by the Institutional Review Board of the Tulane University Medical Center.
Table 1. Mean Levels (±SD) of Study Variables by Race and Sex

<table>
<thead>
<tr>
<th>Race</th>
<th>Sex</th>
<th>Variable</th>
<th>Male (n=325)</th>
<th>Female (n=409)</th>
<th>Male (n=131)</th>
<th>Female (n=175)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td></td>
<td>Age, years</td>
<td>35.9±4.5</td>
<td>35.4±4.5</td>
<td>35.8±4.5</td>
<td>35.3±4.8</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Height, cm</td>
<td>177.8±6.2</td>
<td>163.5±6.3</td>
<td>176.5±6.6</td>
<td>163.3±7.7</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMI, kg/m²</td>
<td>28.6±5.4</td>
<td>28.2±7.1</td>
<td>29.0±7.5</td>
<td>30.3±7.9</td>
<td>&lt;0.01f</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systolic blood pressure, mm Hg</td>
<td>118.4±11.6</td>
<td>111.4±12.1</td>
<td>126.3±15.9</td>
<td>118.6±16.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diastolic blood pressure, mm Hg</td>
<td>80.1±8.1</td>
<td>75.2±8.7</td>
<td>84.7±12.4</td>
<td>79.1±11.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MAP, mm Hg</td>
<td>92.9±6.8</td>
<td>87.3±9.5</td>
<td>98.6±13.0</td>
<td>92.3±12.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total cholesterol/HDL-C</td>
<td>5.0±1.5</td>
<td>4.1±1.3</td>
<td>4.2±1.5</td>
<td>3.5±1.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose, mg/dL</td>
<td>85.8±19.3</td>
<td>81.9±15.2</td>
<td>88.8±31.8</td>
<td>85.4±29.5</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Heart rate, beats/min</td>
<td>67.6±8.9</td>
<td>70.7±9.1</td>
<td>68.8±8.8</td>
<td>71.0±9.6</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carotid IMT, mm</td>
<td>0.76±0.13</td>
<td>0.69±0.10</td>
<td>0.82±0.14</td>
<td>0.75±0.12</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carotid lumen diameter, mm</td>
<td>6.09±0.60</td>
<td>5.43±0.48</td>
<td>6.17±0.75</td>
<td>5.55±0.58</td>
<td>&lt;0.05c</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Height-adjusted diameter, mm/m</td>
<td>3.43±0.34</td>
<td>3.33±0.30</td>
<td>3.50±0.44</td>
<td>3.40±0.36</td>
<td>&lt;0.01f</td>
</tr>
</tbody>
</table>

NS indicates P>0.05; f, females only; w, whites only.

General Examinations

Standardized protocols were used by trained examiners.13 Height and weight were measured twice, and the mean values were used to calculate body mass index (BMI=weight in kilograms divided by the square of the height in meters) as a measure of overall adiposity. Blood pressure was measured in triplicate with a mercury sphygmomanometer by 2 nurses while subjects were seated and relaxed. The first and fifth Korotkoff phases were used to determine systolic and diastolic blood pressure, respectively; means of 6 replicate readings were used. Forced values (140/90 mm Hg) were assigned for systolic and diastolic blood pressure, respectively, to subjects (n=67) who were on medications for hypertension at the time of examination. Mean arterial pressure (MAP) was calculated as diastolic blood pressure+one third pulse pressure. Hypertension was defined as systolic and/or diastolic blood pressure ≥140/90 mm Hg or on antihypertensive medications.

Laboratory Analysis

Subjects were instructed to fast for 12 hours before screening, and the compliance was determined by interview on the morning of examination. Serum cholesterol was determined enzymatically on the Hitachi 902 Automatic Nalyzer (Roche Diagnostics, Indianapolis, Ind). Serum lipoprotein cholesterol levels were analyzed by a combination of heparin–calcium precipitation and agar–agarose gel electrophoresis procedures.14 The laboratory is being monitored for precision and accuracy of lipid measurements by the agency’s surveillance program of the Centers for Disease Control and Prevention, Atlanta, Ga. Plasma glucose was measured by a glucose oxidase method as part of the multiple chemistry profile (SMA20) in the multichannel Olympus Au-5000 Analyzer (Olympus, Lake Success, NY). Intraclass correlation coefficients, a measure of reproducibility of the entire process from blood collection to data processing, between the blind duplicate values (n=103) were 0.98 for total cholesterol, 0.99 for high-density lipoprotein cholesterol (HDL-C), and 0.98 for glucose. Forced values of 240 mg/dL for total cholesterol and 126 mol/dL for glucose were assigned to subjects who were on medications for dyslipidemia (n=26) and diabetes (n=19) at the time of examination, respectively.

Carotid Ultrasonography

Carotid ultrasound measurements were done on a Toshiba Ultrasound instrument (Power Vision Toshiba SSH-380 ultrasound system; Toshiba America Medical Systems, Carrollton, Texas) using a 7.5-MHz linear array transducer. Images were recorded on right and left common carotid according to previously developed protocols for the Atherosclerosis Risk in Communities study.15 Images were recorded on super VHS video tapes and read by certified readers from the Vascular Ultrasound Research Laboratory in Wake Forest using a semiautomatic ultrasound imaging. The common carotid lumen diameter at diastole was measured by M-mode ultrasound. The lumen diameter between the near and far wall intima media interfaces was imaged along the vessel length (ie, the 1-cm segment proximal to the dilation of the carotid bulb) on both sides. Carotid IMT at diastole from the far walls of the common carotid artery on both sides was measured by B-mode ultrasound. The mean values of left- and right-sided lumen diameter and carotid IMT readings were used for the analyses. If bilateral images were not available, the value of one side was used as the mean.

Statistical Methods

All data analyses were performed using SAS 9.1. Total cholesterol/HDL-C ratio was log-transformed to improve the normality of distribution for correlation and regression analyses; however, their mean values in original scales are presented in Table 1 for description. Differences in mean values of study variables between race–sex groups were tested by analysis of covariance models. The correlations of the height-adjusted lumen diameter with carotid IMT and CV risk factors were assessed using Pearson correlation coefficients; the difference in the correlation coefficients between blacks and whites was tested with Fisher’s Z-test. Carotid lumen diameter was adjusted for height by using a ratio of the diameter to height (mm/m) because of their strong correlation.8,11,16 The impact of the correlates of carotid lumen diameter was examined by multivariate regression models by race separately and in the total sample. Trajectories of carotid lumen diameter with CV risk variables in race or sex groups or among hypertensives versus normotensives were estimated using a separate slopes model. The differences in slopes between groups (interaction effects on the lumen diameter) were tested using a homogeneity-of-slopes model.

Results

Table 1 shows the mean levels of study variables by race and sex. Significant race differences were noted in both sexes for blood pressure (whites<blacks), total/HDL-C ratio (whites>blacks), and carotid IMT (whites<blacks); however, the race differences in BMI (whites<blacks), lumen diameter (whites<blacks), and height-adjusted lumen diam-
eter (whites > blacks) were significant only in females. As a group, blacks had greater carotid artery lumen diameter adjusted for height than whites (3.44 mm/m versus 3.37 mm/m, \( P = 0.002 \)) and for males than females (3.45 mm/m versus 3.35 mm/m, \( P < 0.001 \)). Compared with females, males showed higher values of height, blood pressure, total/HDL-C ratio, heart rate, carotid IMT, carotid lumen diameter, and height-adjusted lumen diameter; males had higher glucose than females in whites only. The overall prevalence of hypertension was 16.1% in the total sample. The prevalence was higher in blacks than in whites (25.2% versus 12.1%, \( P < 0.001 \)) and higher in males than in females (20.6% versus 12.5%, \( P < 0.001 \)).

Pearson correlation coefficients of height-adjusted carotid lumen diameter with carotid IMT and CV risk factors are presented in Table 2. BMI and carotid IMT were significantly correlated with the lumen diameter in both races and the total sample. Total cholesterol/HDL-C ratio was correlated with the lumen diameter in whites and the total sample; heart rate in whites; and glucose in whites, males, and the total sample. The correlation coefficients were marginally different between blacks and whites for MAP (\( P = 0.066 \)) and carotid IMT (\( P = 0.095 \)) and between males and females for BMI (\( P = 0.062 \)); the correlation coefficients significantly differed between males and females for MAP (\( P = 0.007 \)).

Standardized regression coefficients of height-adjusted carotid lumen diameter on carotid IMT and CV risk factors are presented in Table 3. BMI and carotid IMT were significantly and positively associated with carotid lumen diameter in both races; sex and heart rate in whites only; and MAP in blacks only. Based on the magnitude of standardized regression coefficients in the total sample, BMI, carotid IMT, MAP, and sex (male > female) were, in that order, associated with the height-adjusted carotid lumen diameter.

Trajectories of carotid lumen diameter with CV risk factor variables by race and sex were examined further in a multivariate model. As shown in Figure 1, although the height-adjusted carotid lumen diameter significantly increased with increasing BMI in both males and females, the slope was significantly steeper in males than in females (difference in slopes: \( P = 0.003 \)). Similarly, males also showed a significantly greater slope of the height-adjusted carotid lumen diameter with increasing MAP than females (difference in slopes: \( P = 0.005 \)). In Figure 2, blacks versus whites showed significantly greater slopes of the height-adjusted carotid lumen diameter with increasing MAP (difference in slopes: \( P = 0.011 \)) and carotid IMT (difference in slopes: \( P = 0.033 \)). In Figure 3, hypertensives versus normo-

### Table 2. Correlations of Height-Adjusted Carotid Lumen Diameter and CV Risk Factors by Race and Sex, Adjusted for Age, Sex (Within Race), Race (Within Sex), and Sex/Race (for the Total Sample)

<table>
<thead>
<tr>
<th></th>
<th>White (n=734)</th>
<th>Black (n=306)</th>
<th>Male (n=456)</th>
<th>Female (n=584)</th>
<th>Total (n=1040)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( r )</td>
<td>( P )</td>
<td>( r )</td>
<td>( P )</td>
<td>( r )</td>
</tr>
<tr>
<td>BMI</td>
<td>0.24</td>
<td>&lt;0.001</td>
<td>0.15</td>
<td>&lt;0.001</td>
<td>0.19†</td>
</tr>
<tr>
<td>MAP</td>
<td>0.15</td>
<td>&lt;0.001</td>
<td>0.27*</td>
<td>&lt;0.001</td>
<td>0.29</td>
</tr>
<tr>
<td>Log-total cholesterol/HDL-C</td>
<td>0.09</td>
<td>0.11</td>
<td>0.08</td>
<td>0.166</td>
<td>0.09</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.09</td>
<td>0.017</td>
<td>0.03</td>
<td>0.640</td>
<td>0.09</td>
</tr>
<tr>
<td>Heart rate</td>
<td>0.09</td>
<td>0.015</td>
<td>0.04</td>
<td>0.950</td>
<td>0.06</td>
</tr>
<tr>
<td>Carotid IMT</td>
<td>0.13</td>
<td>&lt;0.001</td>
<td>0.24*</td>
<td>&lt;0.001</td>
<td>0.20</td>
</tr>
</tbody>
</table>

* \( P < 0.10 \) for race difference; † \( P < 0.01 \) for sex difference. Log indicates log transformation.

### Table 3. Standardized Regression Coefficients of Height-Adjusted Carotid Lumen Diameter on Carotid IMT and CV Risk Factor Variables

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>White (n=734)</th>
<th>Black (n=306)</th>
<th>Total (n=1040)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \beta )</td>
<td>( P )</td>
<td>( \beta )</td>
</tr>
<tr>
<td>Black race</td>
<td>-0.138</td>
<td>&lt;0.001</td>
<td>0.016</td>
</tr>
<tr>
<td>Female sex</td>
<td>-0.046</td>
<td>0.228</td>
<td>-0.053</td>
</tr>
<tr>
<td>Age</td>
<td>0.207</td>
<td>&lt;0.001</td>
<td>0.139</td>
</tr>
<tr>
<td>BMI</td>
<td>0.041</td>
<td>0.330</td>
<td>0.199</td>
</tr>
<tr>
<td>MAP</td>
<td>-0.017</td>
<td>0.667</td>
<td>-0.037</td>
</tr>
<tr>
<td>Log-total cholesterol/HDL-C</td>
<td>0.015</td>
<td>0.683</td>
<td>-0.026</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.097</td>
<td>0.008</td>
<td>-0.006</td>
</tr>
<tr>
<td>Heart rate</td>
<td>0.102</td>
<td>0.011</td>
<td>0.174</td>
</tr>
<tr>
<td>Carotid IMT</td>
<td>0.102</td>
<td>0.011</td>
<td>0.174</td>
</tr>
</tbody>
</table>

Log indicates log transformation.
tensives showed significantly higher levels and greater slope of the height-adjusted carotid lumen diameter with increasing carotid IMT (difference in slopes: $P = 0.038$). The hypertension–carotid IMT interaction did not differ significantly between race or sex groups.

**Discussion**

Arterial remodeling represents changes in vascular cross-sectional area in response to atherosclerosis disease initiation and progression and, therefore, was initially perceived as beneficial. However, luminal enlargement should be viewed with caution, especially in younger adults, because this compensatory process in not unlimited. Consistent with earlier reports, the present study demonstrates that besides carotid IMT, a validated surrogate indicator of subclinical atherosclerosis and future CV risk, traditional CV risk factor variables such as sex, BMI, and MAP that are related to carotid IMT were independently associated with lumen diameter. Of particular interest, the magnitude of associations of lumen diameter with carotid IMT and MAP varied significantly by race; with BMI and MAP by sex; and with carotid IMT by hypertension status. These findings from a community-based cohort of asymptomatic younger adults free from the selection bias of an at-risk population of middle-aged and older adults are indicative of the early phase of the vascular remodeling as part of the natural history of atherosclerosis.

Although carotid IMT, a determinant of the lumen diameter, was significantly higher in blacks than in whites in this as well as previous studies, including our own, race was not an independent predictor of lumen diameter in a multivariate model. Clarkson et al found in an autopsy study that blacks versus whites had larger coronary artery lumina despite having a larger intimal area. Multivariate predictors of lumen area in their study were intimal area, height, race, and history of CV disease. They concluded that such compensatory luminal enlargement in blacks versus whites may account for the relatively less clinical ischemic heart disease observed in blacks. Later studies confirmed these conclusions. Of note, in the current study, the effects of carotid IMT and MAP on lumen diameter were relatively stronger in blacks versus whites, suggesting that the adverse effects of these risk variables on the arterial wall were more than compensated by excess luminal enlargement in this racial group.

With respect to sexual dimorphism in this study cohort, female sex is significantly associated with smaller lumen diameter, independent of carotid IMT and other covariates included in the multivariate model. Earlier studies have shown smaller carotid IMT and lumen diameter in females versus males; whether this could explain the observed relatively lower impacts of BMI and MAP on lumen diameter in females versus males is not clear. It should be noted that severity of coronary artery disease is known to be less in women, especially white women, of reproductive age compared with men; this disparity eventually disappear in postmenopausal woman. Findings from many previous studies supported the estrogen protection hypothesis. Observations on the sex difference in the relationship of BMI and MAP to lumen diameter in this study suggest that sex hormones might be involved in the complex regulation of the vascular remodeling.

![Figure 1. Relationship of height-adjusted common carotid lumen diameter to BMI and MAP by sex.](http://stroke.ahajournals.org/)

![Comparison of slopes: $p=0.003$](http://stroke.ahajournals.org/)

**Figure 1.** Relationship of height-adjusted common carotid lumen diameter to BMI and MAP by sex.
In the current study, BMI was found to be positively associated with enlarged carotid lumen diameter independent of other CV risk variables. Because this study is cross-sectional and observational in nature, it cannot address the issue of causality or underlying mechanisms, but can only suggest possible reasons for the observed relationships. Excess adiposity could induce luminal enlargement through a variety of intermediated factors. These included, among others, impaired arterial compliance, increases in intravascular volume and blood pressure, activation of endothelial dysfunction and the adipose renin–angiotensin–aldosterone system, and excess inflammatory response.29–34

Increased shear stress at intimal thickening of the stenotic site is thought to induce luminal enlargement to normalize the wall shear stress.35 Matrix metalloproteinases generated during disease progression may play a role in vascular remodeling by degrading the extracellular matrix, which can lead to weakening of the arterial wall and the attendant luminal enlargement.36 With respect to blood pressure, sustained excess blood pressure is known to produce mechanical stress and medial degeneration resulting in impaired arterial compliance; and such reduction in compliance of large arteries might bring about a large diastolic lumen diameter, known as caliber increase.37,38 In the current study, the carotid IMT–lumen diameter relationship was significantly stronger in hypertensives than in normotensives, suggesting a synergistic influence of blood pressure and arterial thickening on lumen enlargement. This observation is consistent with the finding from a previous study39 and supports the concepts mentioned.

In conclusion, vascular remodeling, as measured by common carotid artery lumen diameter, is influenced independently by IMT, adiposity, and blood pressure among asymptomatic younger adults in a race- and sex-specific manner. As part of prevention cardiology, future studies are needed to ascertain the potential value of carotid lumen diameter in conjunction with IMT and CV risk factors in identifying risk associated with early subclinical atherosclerosis in younger adults.

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Disclosures
None.

References
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