Ultrasonic Measurement of the Elastic Modulus of the Common Carotid Artery

The Atherosclerosis Risk in Communities (ARIC) Study

Ward A. Riley, PhD; Ralph W. Barnes, PhD; Gregory W. Evans, MS; and Gregory L. Burke, MD, MS

Background and Purpose: The Atherosclerosis Risk in Communities Study is a prospective investigation of the etiology and natural history of atherosclerosis and the etiology of clinical disease in four US communities.

Methods: Noninvasive ultrasonic methods were used to determine mean wall thickness (WT), radius (R), and circumferential arterial strain (CAS) in the left common carotid artery of 3,321 white male and female study participants between the ages of 45 and 64 years. The mean and standard deviation of Young’s elastic modulus (Y) in 5-year age groups were determined for each sex by combining the ultrasonic data with concurrent noninvasive measurements of pulse pressure (PP) in the right brachial artery using the equation Y = (R/WT) × (PP/CAS).

Results: Significant (p=0.0001) age group differences in Y were observed in both sexes, with the mean value increasing from 701 kPa in women and 771 kPa in men in the 45–49-year-old age group to 965 and 983 kPa, respectively, in the 60–64-year-old age group. Significant (p=0.0001) age group differences were also observed for WT, the WT/R ratio, PP, CAS, and the PP/CAS ratio in both sexes. A sex difference in Y was detected (male > female, p=0.0006) only in the 45–49-year-old age group. Significant (p < 0.0001) sex differences were found, with men having a greater lumen diameter calculated as 2 × (R – WT), a greater WT, and a greater 2R in all age groups. The WT/R ratio did not differ in both sexes in all age groups.

Conclusions: Knowledge of the arterial wall elastic modulus and the parameters required for its determination can provide important insight into structural changes occurring within the arterial wall with age and sex, and possibly with the onset of very early arterial disease. (Stroke 1992;23:952–956)

KEY WORDS • carotid artery • risk factors • ultrasonics

The concept of a longitudinal elastic modulus, commonly referred to as Young’s modulus (Y), was introduced during the first decade of the 19th century to describe the aggregate elastic characteristics of arterial wall constituents and structure. Before 1960, nearly all measurements of the elastic moduli of human arteries were performed on excised tissue samples, providing results that one would expect to differ significantly from in situ values due to the geometric, environmental, and structural changes associated with the vessel after excision. With the recent development of noninvasive ultrasonic pulse–echo methods, it became possible to directly determine with high precision two important ratios required to obtain in vivo values of Y associated with the circumferential stretching of the artery wall: the ratio of arterial wall thickness (WT) to radius (R) and the circumferential arterial strain (fractional diameter change) (CAS) occurring during the cardiac cycle. By combining these measures with noninvasive indirect estimates of arterial blood pressure within the examined segments, Y can be calculated. Y differs from other parameters used to define arterial stiffness (e.g., compliance and distensibility) in that WT is required for its determination.

Atherosclerosis is a disease of the artery wall, and a knowledge of Y in a general population sample of predominantly normal individuals can provide an important reference for understanding arterial wall changes that may occur before and during the early stages of the disease. Consequently, Y may be an important parameter for characterizing the arterial wall to study possible links between arterial wall composition and structure and cardiovascular disease risk, as well as for monitoring changes in internal composition and structure during studies of atherosclerosis progression and regression.

The primary objective of this paper is to describe the variation with age and sex, two major cardiovascular disease risk factors, of the mean value of Y in the left common carotid artery in 3,321 white adults between the ages of 45 and 64 years who are participants in the ongoing Atherosclerosis Risk in Communities (ARIC) Study. Future reports will describe results in black
participants and associations of Y with other established risk factors and prevalent cardiovascular disease.

Subjects and Methods
The ARIC Study is a prospective investigation of the etiology and natural history of atherosclerosis and the etiology of clinical disease in four US communities and has been described in detail elsewhere. The ARIC Study also measures variation in cardiovascular risk factors, medical care, and disease by race, sex, place, and time. A probability sample of residents aged 45–64 years is drawn from each community to take part in an extensive evaluation of cardiovascular risk factors and their sequelae. A major component of the evaluation is an ultrasonic examination of the carotid arteries in which ultrasonic pulse-echo techniques are used to measure arterial wall intima plus media thickness and the continuous variation of arterial diameter throughout the cardiac cycle. Resting supine blood pressure is also measured in the right brachial artery at 5-minute intervals during the examination.

For a given material Y is defined as the ratio of stress (force per unit area) to strain (fractional change in linear dimension produced along the direction of the stress). For the case of an arterial segment that approximates a homogeneous thin-walled circular cylinder, Y is defined as \( R/WT \times (PP/CAS) \), where R is the arterial radius, WT is the arterial wall thickness, PP is the pulse pressure within the arterial segment, and CAS is the fractional increase in arterial diameter during the cardiac cycle. The four dimensional parameters in this equation are measured from an ultrasonic examination of a longitudinal section of the left common carotid artery in a 1-cm segment extending from 1 to 2 cm proximal to the tip of the flow divider using standardized ultrasound protocols as part of the ARIC Study.

The presence of large, irregular, lumen-encroaching lesions at this site is infrequent in this probability sample, and identical standard protocols were used on all subjects.

R is one half of the arterial diameter associated with the nearly circular cylindrical surface defined by the media–adventitia boundary. WT is the combined thickness of the intima plus the media. Both R and WT were measured on ultrasonic B-mode images. PP was measured in the right brachial artery with the subject at rest in the supine position. CAS was obtained using echotriangulation techniques to permit the arterial diameter to be measured continuously during the cardiac cycle. This model assumes that the contribution of the adventitia to the overall elastic properties of the artery wall is negligible.

Standard statistical analyses were performed on data obtained from 3,321 participants. Individuals who had missing values for one or more variables required for computing Y were excluded from the analysis. Mean values are reported for each parameter by sex and the 5-year age groups 45–49, 50–54, 55–59, and 60–64 years. Age group and sex differences, and possible interactions, were assessed using PROC GLM of SAS.

Results
Table 1 gives the number of subjects in each age/sex group and the noninvasively determined resting diastolic blood pressure (DBP) and systolic blood pressure (SBP) in the right brachial artery. The number of subjects in each age/sex group ranged from 348 to 571. DBP remained constant with age in both sexes and was significantly \( (p<0.0001) \) higher in men than in women, by about 8 mm Hg. SBP was significantly \( (p<0.0001) \) higher in the older age groups in each sex, with SBP of men significantly \( (p<0.001) \) higher than that of women in all age groups. In the oldest age group, SBP of men was about 5 mm Hg higher than that of women.

Table 2 gives systolic lumen diameter (LD) of the left common carotid artery by 5-year age/sex group. A standard measure for quantifying atherosclerosis from angiography, LD can be determined ultrasonically by measuring WT and 2R and computing the quantity \( 2 \times (R - WT) \). LD was significantly \( (p<0.0001) \) larger in men than in women in all age groups, by about 0.60 mm. Within each sex, LD remained nearly constant with age, increasing very slightly in women.

Table 2 also summarizes data for systolic WT. WT was significantly \( (p<0.0001) \) greater in men than in women in all age groups, by about 0.06 mm. Age groups differed at \( p<0.0001 \) in both sexes, increasing by about 0.12 mm from the youngest to the oldest age group.

Table 3 summarizes data for 2R. This value was significantly \( (p<0.0001) \) greater in men than in women in all age groups, by about 0.80 mm, and increased in both sexes, by 0.50 mm in women and 0.30 mm in men, from the youngest to the oldest age group. Data for the WT/R ratio are also given in Table 3. No sex difference existed in any age group, but age groups differed at \( p<0.0001 \) in both sexes. The WT/R ratio increased by about 0.02 from the youngest to the oldest age group.

Table 1. Elastic Modulus of Carotid Artery

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>N</th>
<th>Diastolic</th>
<th>Systolic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>45–49</td>
<td>571</td>
<td>419</td>
<td>66.9±8.1</td>
</tr>
<tr>
<td>50–54</td>
<td>490</td>
<td>383</td>
<td>68.7±8.8</td>
</tr>
<tr>
<td>55–59</td>
<td>410</td>
<td>352</td>
<td>66.8±8.8</td>
</tr>
<tr>
<td>60–64</td>
<td>348</td>
<td>348</td>
<td>67.4±8.7</td>
</tr>
</tbody>
</table>

Values are mean±SD mm Hg. F, female; M, male. For diastolic blood pressure females<males in all age groups \( (p<0.0001) \); for systolic blood pressure females<males in all age groups \( (p<0.0001) \).
TABLE 3. Average Arterial Diameter and Ratio of Wall Thickness to Radius of Participants in Atherosclerosis Risk in Communities Study

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>Diameter (mm)</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>45-49</td>
<td>6.96±0.61</td>
<td>7.84±0.68</td>
</tr>
<tr>
<td>50-54</td>
<td>7.11±0.63</td>
<td>7.86±0.69</td>
</tr>
<tr>
<td>55-59</td>
<td>7.22±0.64</td>
<td>8.01±0.76</td>
</tr>
<tr>
<td>60-64</td>
<td>7.46±0.66</td>
<td>8.14±0.75</td>
</tr>
</tbody>
</table>

Values are mean±SD. F, female; M, male. For diameter females<males in all age groups (p<0.0001). Small age-sex interaction exists; in females age groups differ at p=0.01, and in males means increase slightly but significantly (p<0.05) between successive age groups, except 45-49=50-54. For ratio age groups differ at p<0.0001 in both sexes; no age-sex interaction exists (p=0.61).

Table 4 summarizes data for brachial PP. PP was significantly (p<0.0131) greater in women than in men in all but the youngest age group, with the difference between sexes being 3.2 mm in the oldest age group. Age groups differed at p<0.0001 in both sexes. PP increased by 11.6 mm Hg in women and 7.7 mm Hg in men from the youngest to the oldest age group. Data for CAS are also summarized in Table 4. A significant (p<0.0001) sex difference existed for CAS only in the youngest age group, with values in women higher than those in men, by 0.004. In the other three age groups differences were of borderline significance in the same direction. Age groups differed at p<0.0001 in both sexes. CAS decreased by 0.010 in women and 0.009 in men from the youngest to the oldest age group.

Table 5 summarizes data for both pressure-strain elastic modulus (PP/CAS) and Y. A significant (p<0.0006) sex difference existed for both PP/CAS and Y only in the youngest age group, with values in men higher than those in women, by about 5 kPa. For PP/CAS, sex differences were of borderline significance in the same direction. Age groups differed at p<0.0001 in both sexes. PP/CAS increased by 58 kPa (38%) in women and 212 kPa (27%) in men from the youngest to the oldest age group. Y increased by 11.6 mm Hg in women and 7.7 mm Hg in men from the youngest to the oldest age group. Y only in the youngest age group, with values in men higher than those in women, by 0.004. In the other three age groups differences were of borderline significance in the same direction. Age groups differed at p<0.0001 in both sexes. CAS decreased by 0.010 in women and 0.009 in men from the youngest to the oldest age group.

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**Discussion**

Noninvasive determination of Y in the common carotid artery requires knowledge of the parameters R, WT in the common carotid artery. 10-16 Other studies in humans and animals have used standard methods to measure PP and noninvasive ultrasonic pulse-echo tracking methods to measure CAS and consequently the PP/CAS ratio. 4-18 We report, from concurrent measurements of all four parameters, the first large population-based, multicenter, in vivo determination of Y in the adult human common carotid artery.

The substantial increase in Y observed with age in both sexes implies a real change in the internal composition and/or structure of the arterial wall. This increase in Y was accompanied by a significant increase in WT. However, arterial diameter increased slightly and appeared to compensate for the increase in WT to maintain a nearly constant LD. Over the same age range, CAS decreased even though PP causing the artery to expand increased. As a result, PP/CAS also increased rapidly with age, at a rate greater than that for Y. Both elastic moduli increased significantly with age in each sex.

However, a significant sex difference in Y was observed only in the youngest age group. Similarly, only in the youngest age group was there a significant sex difference in PP/CAS. While an increase in Y with age is to be expected, the absence of a sex difference in persons above 50 years of age is surprising. This is particularly so if one considers that above 50 years of age there was either a highly significant or borderline significant sex difference in each term in the equation defining Y (i.e., WT, R, PP, and CAS). In addition, DBP and SBP were consistently higher in men than in women. However, values for the first of the two ratios (R/WT) in the defining equation were almost identical for the two sexes in each age group, and values for the second ratio (PP/CAS) demonstrated no difference between the sexes above age 50 years. The absence of a significant sex difference in these ratios in a general population sample of white men and women over 50 years of age is a very interesting observation arising from this study.

That the pressure-strain elastic modulus tends to be greater in men than in women below the age of 50 years is confirmed by previous observations in two younger populations. At a mean age of 16 years, PP/CAS was 67 kPa in males and 62 kPa in females.4 A similar difference of about 5 kPa was also observed in young subjects with a mean age of 13.5 years.12 The lower values of
both Y and PP/CAS in women aged 45–49 years in our study are consistent with these earlier observations if the WT/R ratio in young subjects is also similar in the two sexes. This could suggest a change in arterial wall composition or structure related to menopause that raises values in women to those in men.

The relative constancy of the WT/R ratio in the two sexes, whose arteries demonstrate substantial differences in the absolute values of WT and R, tends to confirm the concept that this ratio evolves within an arterial segment to satisfy a complex combination of physical requirements related to optimal functioning of the arterial wall.22–24 In spite of the fact that WT and 2R are markedly larger in men, the similarity of the WT/R ratio in men and women suggests that it may be a more meaningful parameter than WT for attempting to describe relevant early atherosclerotic changes in arteries.

The increase in the WT/R ratio with age may indicate, within the population sample, an increasing amount of early arterial disease at this site. However, measurements of LD suggest no such increase. In fact, a careful look at the data suggests that there is a slight tendency for LD to increase, rather than decrease, with age. This observation stresses the importance of relying on measurements of the arterial wall (and diameter) rather than LD in attempting to monitor the early stages of atherosclerosis.

As discussed in a previous article,4 blood pressure measured in the brachial artery may not always accurately reflect blood pressure in the common carotid artery. However, comparisons of intra-arterial pressure in the large vessels with brachial artery pressures determined with noninvasive oscillometric methods are in generally good agreement.25

The ARIC Study cohort was a population-based sample selected by probability sampling within four communities. Details of the sampling frame and methods have been described.6 There were no exclusion criteria, although severely ill individuals or those with conditions that limit mobility may have been more likely to refuse participation in the clinical examination. In addition, participants who did not yield acceptable measurements of all four parameters have, of necessity, been excluded from the analyses described here. In general, the participants with missing data were somewhat older and less healthy. Thus, the means and standard deviations of the parameters reported here may be slightly biased. Despite these limitations, the ARIC Study cohort provides an excellent opportunity to assess the elastic properties of the carotid arteries in a large population-based sample within specific age and sex groups.

It is important to emphasize that all of the age-related results described here are cross sectional and not descriptions of longitudinal changes within individuals. The standard methods used to measure the relevant parameters (e.g., WT and PP/CAS) are highly reproducible, however, and can be used to monitor changes in individuals over time. Mean absolute differences in measurements of carotid artery WT from blinded repeat studies have ranged from approximately 0.08 to 0.14 mm.7,26 This is typically <3% of the mean LD and approximately the magnitude of the increase observed in this population from the youngest to the oldest age group. Mean differences in similar repeated measurements of PP/CAS have ranged from approximately 10 to 20 kPa in younger and older subjects.4,13 This is typically <15% of the mean value of PP/CAS observed in a 55-year-old subject and is approximately one third of the increase in the mean value observed in this population from the youngest to the oldest age group. A detailed analysis of quality control in a subset of the ARIC Study population that will precisely estimate within- and between-observer variability related to these parameters is currently in progress.

These multiple observations on the ARIC Study population demonstrate that a variety of potentially important physical changes occur in arterial dimensions and wall stiffness within a general population sample while LD remains unaffected. A better understanding of the mechanisms producing these changes and how they might be modified could lead to new insights into the very early stages of atherosclerotic disease.

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