Estimation of Arterial Stiffness, Compliance, and Distensibility From M-Mode Ultrasound Measurements of the Common Carotid Artery

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Background and Purpose Arterial stiffness may indicate early vascular changes that predispose to the development of major vascular disease. The repeatability of a variety of indices of arterial stiffness calculated from a standard carotid arterial M-mode ultrasound image was investigated.

Methods Twenty-six asymptomatic normal subjects were imaged and had blood pressure recordings on each of two separate occasions at least 1 day apart. Using a computer-assisted method, the maximum and minimum internal diameter and average wall thickness of the right common carotid artery were measured over several cardiac cycles, and the following indices of arterial stiffness and distensibility (compliance) were derived: the pressure-strain elastic modulus (Ep), Young's modulus (E), cross-sectional compliance (CC), and the distensibility coefficient (DC).

Results The repeatability of these measures, expressed as coefficients of variation, was as follows: Ep, 18%; E, 24%; CC, 14%; and DC, 13%. In another group of 20 subjects, the coefficient of variation for repeat examination by different sonographers was Ep, 19%; E, 20%; CC, 14%; and DC, 17% and for the one sonographer using two ultrasound machines was Ep, 13%; E, 13%; CC, 11%; and DC, 13%. These values indicate a moderate level of repeatability. In a univariate analysis each of these indices was significantly related to increasing age (Ep=1.0+12.9×AGE, r=−.80; E=314.5+13.9×AGE, r=−.48; CC=22.6−0.26×AGE, r=−.63; DC=64.0−0.65×AGE, r=−.78) but not to wall thickness (all P>0.7). Using multiple regression techniques to adjust for age, wall thickness is a significant predictor of distensibility (P=0.017), cross-sectional compliance (P<0.001), and the pressure-strain elastic modulus (P=0.019). Because Young's modulus is calculated from wall thickness, it could not be included in the multivariate analysis.

Conclusions We conclude that estimates of carotid artery distensibility and cross-sectional compliance derived from M-mode ultrasound recordings are moderately repeatable and may provide useful additional end points for trials of atherosclerotic progression. (Stroke. 1994;25:11-16.)

Key Words • atherosclerosis • carotid arteries • ultrasonics

Arterial stiffness\(^1\) and its reciprocal, arterial distensibility (or compliance)\(^2\), may provide indices of early vascular changes that predispose to the development of major vascular disease. Localized increases in wall stiffness have been documented in areas of artery adjacent to regions of plaque.\(^3\) Men with angiographically verified coronary artery disease have been shown to have stiffer arteries than control subjects.\(^4\)–\(^6\) Patients with a history of myocardial infarction have been shown to have increased arterial stiffness,\(^7\) as have their offspring.\(^8\) Risk factors for vascular disease including age,\(^9\)–\(^10\) blood pressure,\(^11\)–\(^13\) blood cholesterol,\(^8\) and diabetes\(^8\) have all been shown to be positively associated with arterial stiffness. Each of these observations is therefore consistent with the hypothesis that increased arterial stiffness (and reduced compliance) is a precursor, or at least a predictor, of atherosclerotic disease. Unlike established atherosclerotic disease, however, increased arterial stiffness may be reversed quickly by pharmacologic and dietary interventions. In hypertensive subjects, it has been reported that calcium antagonists,\(^2\)–\(^4\) \(\beta\)-adrenoceptor blockers,\(^4\) and angiotensin converting enzyme inhibition\(^15\)–\(^16\) can reduce arterial stiffness. In normotensive subjects it has been suggested that sodium restriction may also reduce arterial stiffness\(^17\) and that reversible increases in arterial compliance can be seen after a brief period of exercise training.\(^18\)

More evidence about the prognostic significance of increased arterial stiffness and the effects of interventions on this parameter would be useful. However, the conduct of appropriate large-scale clinical and epidemiological studies has been hampered by the absence of simple measurement techniques. Previous studies have used a variety of measurement methods including applanation tonometry,\(^19\) multigated pulsed Doppler,\(^20\)–\(^22\) phase-locked echo tracking,\(^10\) magnetic resonance imaging,\(^6\) intravascular ultrasound,\(^22\) B-mode ultrasound,\(^3\) and pulsed Doppler velocimetry,\(^11\)–\(^15\),\(^23\)–\(^24\) each of which requires special equipment and training available in only a few centers. For this reason we have assessed the usefulness of M-mode ultrasonography of the carotid artery for assessment of arterial stiffness and compliance. This methodology could be applied in most cardiology or radiology departments. Moreover, because B-mode ultrasound measurements of carotid artery wall thickness and plaque prevalence are already being collected in numerous epidemiological studies\(^25\)–\(^27\) and randomized trials,\(^28\)–\(^29\) M-mode ultrasound measurements of arterial stiffness and compliance could potentially provide useful additional end points with little extra effort.

In this study we sought to determine the reproducibility of M-mode measurements of systolic and diastolic
diameters of the right carotid artery and of several calculated indices of arterial stiffness and compliance. We also sought to determine whether these indices were related to age and artery wall thickness in a manner consistent with their being valid measurements of arterial stiffness and compliance.

Subjects and Methods

Twenty-six asymptomatic subjects (18 women; mean age, 40 years; range, 22 to 56 years) were examined by one ultrasonographer on two occasions at least 1 day but not more than 4 weeks apart. Before ultrasonography, after 5 minutes’ rest in a semidarkened room, two blood pressure recordings were made from the right arm of the supine subject using a mercury sphygmomanometer. A region 1.5 cm proximal to the origin of the bulb of the right common carotid artery was identified using B-mode ultrasonography. The transducer was manipulated such that the near wall of the carotid artery was parallel to the transducer footprint and the lumen maximized in the longitudinal plane. An M-mode recording at 50 mm/s was made with the M-mode cursor perpendicular to the vessel walls, as identified using B-mode (10-MHz single crystal, mechanical sector transducer, ATL-UM8). Three cardiac cycles were recorded onto videotape and also digitized on-line for later measurement. The sonographer maintained sufficient pressure on the artery to allow acoustic coupling without compressing the artery. After the examination, and with the patient remaining supine, two additional blood pressure readings were made. Average systolic and diastolic blood pressure readings were calculated from four readings taken before and after the ultrasound scan. This entire procedure was repeated at the second visit.

To estimate the reproducibility of measurements made from images collected by two sonographers and to compare measurements made on different ultrasound machines, an additional group of 20 subjects (mean age, 55 years; range, 41 to 64 years) was studied. Images were studied by two sonographers within 19 days (mean, 7 days) of each other. A third sonographer imaged the same patients twice, at least 7 days apart, once using either an ATL-UM8 (10-MHz transducer) or an ACUSON 128 (7-MHz transducer) on the first visit and then the other machine at the second visit. Regular maintenance and quality assurance checks using a phantom ensured that the ultrasound machines were performing to the manufacturer’s specifications.

The digitized M-mode was analyzed off-line using a locally developed computer program. Each image was recalled (magnification x5) and the distance between two successive R waves measured. This distance was divided into 10 equal sections, and the measurer was able to select lumen-intima interfaces for the near and far walls of the carotid artery by positioning a cursor over the point on a computer-generated grid. The cursor was free to vary vertically, but not horizontally, along this grid line (Fig 1). Thus, for each individual the cardiac cycle was divided into tenths, and at each tenth the distance between the lumen-intima interface for the near and far walls was calculated and maximum and minimum lumen interfaces detected. We have previously identified a very close association between the ultrasound representation of the lumen and the actual lumen, measured with electronic calipers, in 10 bovine arteries scanned in a water bath (95% confidence interval [CI] of the difference between caliper and ultrasound, −0.09 to 0.75 mm). Wall thickness of the far wall was measured from B-mode and best represents the combined thicknesses of the intima, media, and the adventitia. The coefficient of variation of measurements of wall thickness is 7.2% for repeated visits (Gamble et al, unpublished data, 1994).

From these measurements the following parameters were estimated: (1) distensibility: the change in carotid artery diameter for a change in arterial blood pressure relative to the average diameter; and (4) Young’s modulus: artery stiffness per centimeter of wall thickness. Because only the far wall of the carotid artery can be validly measured with B-mode ultrasound, this was used to provide an estimate of wall thickness. These parameters were calculated as:

\[
\text{Distensibility Coefficient (DC)} = \frac{\Delta dd/dL}{\Delta p}
\]

\[
\text{Cross-sectional Compliance (CC)} = \frac{\Delta dd/\pi d^2}{2 \Delta p}
\]

\[
\text{Pressure-Strain Elastic Modulus (Ep)} = \frac{\Delta p}{\Delta d} D
\]

\[
\text{Young’s Modulus (E)} = \frac{D}{\Delta d} h
\]

where \(\Delta d\) is the change in diameter, \(d\) is the systolic diameter, \(D\) is the average diameter of the artery, \(h\) is the arterial wall...
thickness, and \( \Delta p \) is the difference between the average systolic and the average diastolic blood pressures. Each parameter was calculated for each of the cardiac cycles and averaged for each subject.

Data were analyzed using the statistical package SAS.\(^2\) Spearman's rank correlation coefficient, coefficients of variation and reproducibility (95% confidence intervals),\(^3\) and simple absolute and mean differences were used to compare intermeasurer and intrameasurer reproducibility. A sample size of 26 would provide more than 80% power (\( \alpha = 0.05 \))\(^4\) to detect "almost perfect"\(^5\) agreement between pairs of measurements. Intraclass correlation coefficients were calculated from the between- and within-person mean squares for a one-way ANOVA.\(^6\) The standard deviation of the intermeasurer error was calculated as the standard deviation of the differences over \( \sqrt{n} \). Stepwise and maximum \( R^2 \) techniques were used to fit multiple regression models of the data. A 5% significance level was maintained throughout these analyses.

**Results**

The associations between measurements of systolic and diastolic lumen diameters made at the first and second visits and the least-squares regression lines are
plotted in Fig 2. These show a close linear association between replicate measurements of each parameter. The intraclass correlation coefficients for systolic and diastolic diameters were both >0.8, and the coefficients of variation were both approximately 6% (Table 1). For these two parameters, the mean absolute difference between measurements at the first and second visits was only 0.04 cm (approximately 6% to 7%). Intrameasurer reproducibility assessed by repeat measurements of all scans recorded at the first visit was high, with the correlation coefficients >0.8 for both systolic and diastolic diameters. Intermeasurer reproducibility assessed by comparison of measurements from the same scans made by two observers yielded similar correlation coefficients (>0.8).

The associations between replicate estimates of the four indices of stiffness or compliance at the first and second visits and the least-squares regression lines are also plotted in Fig 2. There were significant linear relations of moderate magnitude (r=0.41 to 0.73) for each of the parameters (Table 2). The coefficients of variation for the replicate measurements ranged from 12.5% for the distensibility coefficient to 24.2% for Young’s modulus. Accordingly, the mean absolute difference between the first and second estimates of these parameters ranged from 21% for the distensibility coefficient to 34% for Young’s modulus.

The coefficients of variation for measurements made from images collected from the same person by different sonographers were 18.5%, 20.2%, 14%, and 17% for the pressure-strain elastic modulus, Young’s modulus, the distensibility coefficient, and cross-sectional compliance, respectively. Comparison of the difference in images collected by one sonographer on two ultrasound machines produced coefficients of variation of 13.1%, 12.8%, 11.3%, and 13% for the pressure-strain elastic modulus, Young’s modulus, the distensibility coefficient, and cross-sectional compliance, respectively.

Both the pressure-strain elastic modulus and Young’s modulus increased significantly with increasing age (Ep=1.0+12.9xAGE, r=.80; E=314.5+13.9xAGE, r=.48), whereas the distensibility coefficient and cross-sectional compliance decreased significantly with increasing age (DC=64.0+0.67xAGE, r=.78; CC=22.6−0.26xAGE, r=−.63). Carotid artery wall thickness was not significantly correlated with any of the stiffness or compliance indices (all P>0.47). Wall thickness was, however, found to be a significant independent predictor of the distensibility coefficient, cross-sectional compliance, and the pressure-strain elastic modulus when included in a multiple regression model that adjusted for age (all P<0.017). The association with Young’s modulus was not examined because this index is calculated from wall thickness.

**Discussion**

The results of this study demonstrate that systolic and diastolic lumen diameters of the common carotid artery can be measured reproducibly with M-mode ultrasound using standard equipment and techniques. Reproducibility is not affected by using different sonographers or different ultrasound machines. Correlation coefficients for replicate scans and replicate measurements by the same or different observers were all approximately 0.8 or greater. The coefficients of variation for the lumen diameters from repeated scans were both approximately 6%. The reproducibility of the four indices of arterial stiffness or compliance was also reasonable, although less than that for the lumen diameters themselves. Because each of these indices is calculated from blood pressure as well as lumen diameter (plus arterial wall thickness in the case of Young’s modulus), their reproducibility reflects the sum of the variability of the constituents (which is necessarily greater than the variability of any one constituent, such as lumen diameter, alone). An additional source of variation results from local irregularities in arterial stiffness. Barth et al have demonstrated increased arterial stiffness in areas adjacent to plaques. The M-mode method can only measure dimensions in one region of the artery at a time, although by using B-mode to position the cursor it is possible to obtain consistent sampling. Thus, careful comparison of regions adjacent to plaques or examination of early atherosclerotic disease at regions where plaque development is likely, such as the carotid bifurcation, is possible. An advantage in using M-mode to detect systolic and diastolic diameters is that only a single image needs to be captured, stored, and measured. To obtain the same information from B-mode would require sequential images to be captured throughout the cardiac cycle and compared with one another.

The coefficients of variation for the four indices studied indicate that within individuals only marked changes in arterial stiffness or compliance (greater than 25% to 50%) could be detected reliably with this method. However, small differences between individuals in stiffness or compliance (10%) could be detected reliably in studies involving just a few hundred participants. Clinical and epidemiological studies of carotid artery wall thickness measured with B-mode ultrasound generally require the involvement of at least several hundred participants to detect plausible treatment ef-
Table 2. Estimates of the Reproducibility of Four Indices of Arterial Stiffness or Compliance Calculated From M-Mode Ultrasound Measurements of the Right Common Carotid Artery

<table>
<thead>
<tr>
<th></th>
<th>Visit 1</th>
<th>Visit 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young's modulus, kPa/cm</td>
<td>885.5±86.3</td>
<td>846.4±73.7</td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean difference</td>
<td>865.9±68.8</td>
<td></td>
</tr>
<tr>
<td>Mean absolute difference</td>
<td>39.1±82.7</td>
<td></td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td>±113.9</td>
<td></td>
</tr>
<tr>
<td>Coefficient of variation</td>
<td>24.2%</td>
<td></td>
</tr>
<tr>
<td>Pressure-strain elastic modulus, kPa</td>
<td>54.7±3.6</td>
<td>51.6±3.5</td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean difference</td>
<td>53.1±3.0</td>
<td></td>
</tr>
<tr>
<td>Mean absolute difference</td>
<td>3.1±3.9</td>
<td></td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td>±5.3</td>
<td></td>
</tr>
<tr>
<td>Coefficient of variation</td>
<td>18.4%</td>
<td></td>
</tr>
<tr>
<td>Distensibility coefficient, 10^-3/kPa</td>
<td>36.1±2.1</td>
<td>38.3±2.3</td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean difference</td>
<td>37.2±2.0</td>
<td></td>
</tr>
<tr>
<td>Mean absolute difference</td>
<td>−2.2±2.0</td>
<td></td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td>±2.5</td>
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<tr>
<td>Coefficient of variation</td>
<td>12.5%</td>
<td></td>
</tr>
<tr>
<td>Cross-sectional compliance, 10^-7m^2/kPa</td>
<td>12.2±1.1</td>
<td>12.3±1.0</td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean difference</td>
<td>12.2±1.0</td>
<td></td>
</tr>
<tr>
<td>Mean absolute difference</td>
<td>−0.03±0.8</td>
<td></td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td>±0.5</td>
<td></td>
</tr>
<tr>
<td>Coefficient of variation</td>
<td>14.4%</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SEM where indicated. Difference and pooled data were calculated for each subject (n=26).

Effects. Therefore, with little extra effort, these studies could provide useful additional data from M-mode ultrasound on the determinants and consequences of increased arterial stiffness and reduced compliance and the effects of treatments, including reduction of blood pressure and blood cholesterol.

Although this study was not designed to assess directly the validity of these indices of arterial distensibility and compliance, the results do provide indirect evidence of relevance to this. The observations that the pressure-strain elastic modulus and Young's modulus were directly related to age, while the distensibility coefficient and cross-sectional compliance were inversely related to age, are consistent with other evidence obtained with various techniques indicating that arterial stiffness increases and compliance decreases with age. Moreover, the observations that the pressure-strain elastic modulus was positively related to carotid artery wall thickness, while the distensibility coefficient and cross-sectional compliance were inversely related to carotid artery wall thickness after adjustment for age, are consistent with other evidence that suggests that increased arterial stiffness is the result of changes in the composition of the artery wall. Taken together these results suggest that the carotid M-mode–derived indices of arterial stiffness and compliance are valid. However, studies comparing these indices with those derived from other methods such as applanation tonometry or pulsed Doppler velocimetry would be useful to further establish the validity of this simple method.

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References


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