Quantitative Ultrasound Pulsation Study in Human Carotid Artery Disease

Jacques D. Barth, David H. Blankenhorn, Emily Wickham, June Y. Lai, H.P. Chin, and Robert H. Selzer

Pulsation in the human carotid artery during two complete cardiac cycles was studied by using computer digitized video-frames from B-mode ultrasound images. Eight patients with identifiable atherosclerotic lesions in the common carotid immediately proximal to the bulb area were studied. Diameter, strain, and elastic modulus were compared between lesion site and an adjacent reference segment 1 or 2 cm proximal to the bulb. As controls, nine patients without identifiable lesions were analyzed. The results indicate a significantly wider diameter ($p<0.01$) at the proximal reference site in patients with lesions as compared to comparable segments in control patients. The strain was significantly lower ($p<0.05$), whereas the elastic modulus was significantly higher ($p<0.05$), at the lesion site as compared to the proximal reference sites in patients with lesions. These results may indicate that an initial dilation of the carotid artery followed by loss of wall flexibility may be associated with atherosclerotic lesion formation.

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Diagnosis of carotid artery disease by lesion tracking methods can be performed using noninvasive imaging techniques. Although a number of studies have compared B-mode ultrasound images in various stages of symptomatic carotid artery disease, no study has assessed the change in pulsation during the cardiac cycle in asymptomatic patients at different stages of atherosclerotic disease. Atherosclerotic carotid lesions may vary widely in morphology and composition, and noninvasive quantitation of individual lesion characteristics would be useful. We studied pulsatile effects in the common carotid artery using digitized quantitative measurements. Pulsation at lesion sites in the common carotid immediately below the bulb was compared with pulsation at a proximal reference site located within 2 cm in the same vessel and to pulsation in similar sites from patients without visible lesions. These properties were measured to determine if different patterns of pulsation may be present for patients with and those without visible lesions.

Methods

Patients

The patients who participated in this study represent a subset of patients who participated in the Cholesterol Lowering Atherosclerosis Study (CLAS), a lipid-lowering trial that studied sequential angiographic data. They were men who had had aortocoronary bypass grafts. All patients were current nonsmokers, had normal blood pressures, and were not suffering from cerebrovascular disease. The average blood pressure of the eight subjects with visible lesions (120/78 mm Hg) was not significantly different from that of the nine subjects without visible lesions (115/75 mm Hg). During the CLAS trial routine, ultrasound B-mode scans were performed at 3-month intervals on the right carotid artery. Eight patients with discrete carotid lesions clearly visualized on the video taped scans were identified. Reference areas 1 to 2 cm proximal to the lesion that had a normal appearance were also analyzed. Nine patients without visible lesions were selected as controls. Research protocols and informed consent forms for all subjects in this study were approved by the University of Southern California–Los Angeles County Medical Center Institutional Review Board.

Ultrasound Image Processing

B-mode scanning was performed using a BioDynamics Biosound instrument with a mechanically assisted and positioned 4-inch transducer with a 9 MHz central frequency. Right carotid longitudinal views were recorded at 30 frames per second on 3/4 inch video tape. Longitudinal views were selected because the computer edge detection methods performed more reliably than with cross-sectional views.

A systematic distortion of the image occurs with the Biodynamics ultrasound system because of the fan-shaped ultrasound scanning pattern that is used to obtain the image. A longitudinal scan of a straight uniform cylinder produces an image that is curved, with the top and bottom of the cylinder wider than the middle. To minimize this error, the carotid measurements were made near the center portion of the image whenever possible.

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Of the 30 segments measured, 27 were within the center two-thirds of the image. Measurements applied to phantom images indicate that the maximum error in size for an 8 mm vessel is approximately 0.1 mm at lines one-sixth of the distance from the top and the bottom of the image and 0.2 mm at the extreme top and bottom.

An ultrasound phantom containing three 1 cm reference vessels at tissue depths that bracket the in vivo depth of the human common carotid artery was imaged each scanning day for image quality control. The intended function of this phantom was to provide an object of known size that could be measured and then used to convert ultrasound images to their actual size. A single scaling constant obtained from this phantom was applied to all images. It was discovered that in the 3-year time period during which the patients were scanned, the phantom decreased approximately 5% due to evaporation of contrast material. As a result, phantom images could not be used to separately convert each image to its actual size. The frames were digitized from video tape using a Spatial Data Model 300 Eyecom III digitizer (Spatial Data, Santa Barbara, CA), a Sony 3/4 inch video cassette recorder BVU-820, and a Sony Digital Time Base Corrector BVT-810 (Sony Broadcast Products, San Jose, CA).

The determination of the diameters of the arterial wall segments began with enhancement of the wall edges. The digitized B-mode image (Figure 1) was initially smoothed with a pixel-averaging filter to reduce speckle noise. The horizontal black line in the right-hand portion of the image is a pointer placed by the ultrasound technician during the original examination to flag a carotid lesion. Next, to sharpen the wall edges, a modified version of a variance filter developed by Kuwahara et al. was applied to the smoothed image (Figure 2). As part of the edge detection process, three points were supplied on the enhanced image by the computer operator. Two points indicated the starting edge location for the shallow and deep walls and the third point indicated the length of the segment of interest. The wall edges were automatically detected using a gradient calculation along the length of the segment beginning at the starting location provided by the operator. Figure 3 illustrates the detected edges for a lesion site. The detected edges of the lesion are also shown. The lumen diameter was computed from the
detected edges as the average of 100 measurements along the vessel.

The diameters were measured on every third frame, representing 0.1 second time intervals, for two complete cardiac cycles. A plot of the vessel diameter at a lesion site for two cardiac cycles is shown in Figure 4. The cyclic variation in residual lumen diameter as measured from the shallow wall to the lesion surface is also shown plotted in this figure. A three-point smoothing filter has been applied to the measurements before plotting.

The strain and elastic modulus (Ep) were calculated according to the following formulas:

\[
\text{Strain} = \frac{\text{systolic diameter} - \text{diastolic diameter}}{\text{diastolic diameter}}
\]

\[
\text{Ep} = \frac{\text{systolic blood pressure} - \text{diastolic blood pressure}}{\text{strain}}
\]

Blood pressure (BP) values were derived from the brachial noninvasive artery blood pressure values in kPa recorded on the same visit that the ultrasound scan was performed.

The maximum wall velocity during vessel expansion was also calculated as the time derivative of the diameter measurements.

**Statistics**

The patients' group characteristics were analyzed by using an independent Student's t test. The entry values represent the means of the first three CLAS screening visits. The differences in mean diameters, strain, Ep, and maximum wall velocity between lesion and proximal reference sites in lesion patients were tested using a paired t test. Comparisons between reference sites in the lesion and control patients were tested using independent t tests. As it was hypothesized that values for Ep would be significantly higher at the lesion site as compared to a reference site, one-sided hypotheses were used in Ep analyses. All other hypotheses were two-sided. Significance levels were set at 0.05 for all tests. All testing utilized parametric methods available in a standard statistical programming package.

**Results**

Table 1 summarizes the data on diameters, strain, Ep, and maximal wall velocity for all subjects. The patients with lesions showed significantly higher Ep values at the lesion sites as compared to the proximal reference areas (p<0.05). Strain was found to be significantly lower at the lesion area when compared to the proximal nonlesion sites in the same subjects (p<0.05). No significant differences in diameters were found between lesion sites and proximal reference areas during systole and diastole. A comparison between subjects with and those without lesions showed a significant difference in diameter both for systole (p<0.01) and diastole (p<0.01). No significant differences were found for maximal wall velocity (maximum rate of diameter change) (Table 1).

The distribution of measurement locations in subjects with lesions was 78% at the midcommon carotid artery and 22% at the upper common. For the subjects without visible lesions, it was 75% at midcommon and 25% at upper common. A two-factor analysis of variance was performed to determine if, after controlling for location site, a significant difference in diameter between the two

<table>
<thead>
<tr>
<th>Measured quantity</th>
<th>Patients (n=8)</th>
<th>Controls (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lesion site</td>
<td>Proximal site</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>7.68 (0.32)</td>
<td>7.47 (0.30)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>7.44 (0.29)</td>
<td>7.13 (0.28)</td>
</tr>
<tr>
<td>Strain (%)</td>
<td>3.16 (0.43)*</td>
<td>4.78 (0.52)</td>
</tr>
<tr>
<td>Ep (kPa)</td>
<td>208.6 (32.4)*</td>
<td>131.6 (16.1)</td>
</tr>
<tr>
<td>Maximal wall velocity (mm/sec)</td>
<td>102.5 (14.4)</td>
<td>130.0 (14.9)</td>
</tr>
</tbody>
</table>

Values are means±SEM.

Ep=elastic modulus.

*p<0.05, †p<0.01.
subject groups was demonstrated. Significant differences were still found for both systolic (p=0.001) and diastolic diameters (p=0.001). Therefore, differences in diameters were due to subject classification, rather than to arterial location of measurement.

**Discussion**

The purpose of the study was to assess whether the pulsatile variation during systole and diastole shows different patterns at different stages of carotid atherosclerosis. We used a quantitative digitized method that minimizes observer bias in diameter measurements.

All patients were asymptomatic for cerebrovascular disease, were nonsmokers, and had normal blood pressures. The mean age for patients with lesions was 56.6±1.2 (SEM) and the mean age for patients without lesions was 51.7±2.0 (SEM). From the significantly wider diameters in the lesion patients for both systole and diastole, we infer that dilation may occur as an adaptation to progression of asymptomatic lesions. Such a compensatory enlargement of coronary arteries has recently been reported. Our findings suggest a similar mechanism for the carotid artery.

After an initial adaptation of dilation, loss of flexibility, as represented by significantly higher Ep values in the lesion sites compared to reference nonlesion sites, may occur. Although a loss of flexibility could result in an alteration of maximum wall velocity at lesion sites, such an effect was not seen. This may be due to the fact that the maximum wall velocity measurement is less accurate than the Ep measurements.

Long-term studies with serial observations are indicated to investigate these aspects of the natural history of atherosclerosis. The method we describe appears suitable because it is noninvasive and thus can be repeated as frequently as needed.

From these observations, the following inference can be made regarding early-to-moderate advanced carotid atherosclerosis: an initial adaptation to progression of atherosclerosis is dilation. With further development of disease, a loss of vascular wall flexibility may occur.

**References**


Index Terms: B-mode ultrasound • carotid artery disease • image processing • atherosclerosis • cardiac pulsation
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