Effect of Age on Arterial Distensibility in Asymptomatic Humans

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This report describes a noninvasive method by which the volume distensibility of forearm arteries can be calculated from direct measurements of pulse wave velocity. Such measurements are made at a variety of transmural arterial pressures (TMP) accomplished by placing the forearm in a cylinder and changing the pressures within. This technique eliminates arterial blood pressure as a variable, which strongly influences arterial distensibility. We studied 48 asymptomatic men and women, ages 21 to 98 years. There was considerable scatter, but significant positive relationships were demonstrated between increasing arterial distensibility and age at ambient and lower TMPs. This finding can be explained by an age-related reduction in arterial luminal diameter and an increase in arterial wall thickness which reduces arterial wall tension and more than offsets the increased stiffness produced by changes in wall composition. In six subjects, pulse tracings were simultaneously recorded on paper and analog tape. The taped curves were digitized and subjected to Fourier analysis to determine the wave velocity of individual harmonics. The characteristic wave velocity was defined and found comparable to the hand method used in the same beats (regression coefficient = + 0.97). These data indicate that the automatic and manual methods measured the same variable. (Arteriosclerosis 3:199–205, May/June 1983)

The physical characteristics of the arterial tree have important effects on overall circulatory function. Arterial stiffness partially determines the arterial pulse shape, arterial pressure, the dissipation of cardiac energy, and impedance to left ventricular output, which in turn influence cardiac output and individual organ flows. These relationships have been well documented from studies in animals1–5 but methodologic problems have hindered analogous studies in humans. Aortic input impedance has been measured in patients6–11 but this requires catheterization of the central aorta and complex computations using simultaneously recorded pressure and flow curves. A number of noninvasive methods have also been described which assess the arterial distensibility of peripheral arteries and which are more applicable to the study of larger numbers of patients.12–19 The results have been variable, and none of these techniques has emerged as a reference method against which newer measurements can be compared.

This report describes the calculation of forearm arterial distensibility from direct measurements of brachial to radial pulse wave velocity. Intraarterial blood pressure has been eliminated as a variable by repeating the measurements at transmural arterial pressures above and below ambient pressure. This was accomplished by measuring pulse wave velocity with the forearm encased in an air-filled plastic cylinder within which the pressure was varied. Pulse wave velocities, measured by hand from the recorded curves, were found to be comparable, in a limited number of subjects, with the characteristic wave velocity obtained from Fourier analysis of the same pulses recorded on analog tape. The manual method then was applied to a series of asymptomatic individuals of widely disparate ages to seek trends in calculated arterial distensibility.
Methods

Pulse wave velocity measurements were carried out in 24 male and 24 female asymptomatic, normotensive subjects ranging in age from 21 to 98 years. There were approximately three men and three women in each of the eight decades represented. The subjects were recruited from the ranks of medical students, physicians, technicians, nurses, a nursing home unit that is part of this hospital, and from residents of nearby senior citizen housing.

After measuring the blood pressure (cuff method) in both arms for parity, we placed Pixie strain gauges imbedded in plastic (Endevo Corporation, San Juan Capistrano, California), over the right brachial artery in the antecubital fossa and right radial artery at the wrist. Each gauge was made one arm of a Wheatstone bridge, the balanced bridge outputs were amplified (Model VR6, Electronics for Medicine, White Plains, New York), and the radial dilation waves of both brachial and radial arteries were displayed on an oscilloscope. Gauge positions were adjusted until distortion-free pulse waves were obtained, and gauge locations were maintained by encircling soft elastic bands. Satisfactory pulse curves were then recorded on ultraviolet sensitive paper at a speed of 250 mm/sec (Honeywell Visicorder, Model 1508, Denver, Colorado).

With the gauges in place, the arm was encased within a large plastic cylinder with elbow and wrist extended. The cylinder was closed at one end and bound to the upper arm at the other with a soft rubber sleeve. To minimize pressure loss, the sleeve was covered with an encircling blood pressure cuff which was inflated, when cylinder pressures were positive, to pressures just higher than those within the cylinder. Cylinder pressures were varied in 10 mm Hg increments using an industrial vacuum cleaner and an adjustable leak. The pressure within the cylinder was monitored through a small port using a mercury U-tube. Altered cylinder pressures were established for 30 seconds to 1 minute before pulse waves were recorded, and ambient pressures were allowed to return for several minutes between runs. It was usually possible to raise the cylinder pressure 50 mm Hg, and lower it 80 mm Hg without undue distortion of the wave form. At the conclusion of each study, the distance between the metal recording extension of each gauge was measured by running a strip of adhesive paper tape over the volar surface of the forearm and finding the shortest distance between the skin indentation points. The position of the two gauge arm extensions were marked on the tape and the tape was removed. The strip of tape was then placed on a flat surface and the distance between the marks was measured.

The linearity of the Pixie strain gauges was tested by applying known forces to the gauge arm. The gauges were found to be linear from zero force to fracture of the gauge element. The frequency response of the gauges was also tested. There was an average of 5% loss of signal amplitude at frequencies up to 20 cycles/second. Transmission of positive and negative pressures from an air-filled cylinder to the inside of the forearm has been tested by others, found to be faithful, and was not repeated.20, 21

Since the characteristic wave velocity of the pulse wave represents the velocity of travel of its higher frequency components, and since the pulse curve upstroke contains high frequency information, points on the brachial and radial upstrokes at 10% of the pulse amplitude were arbitrarily chosen to mark the arrival time of the pulses. The time interval between these two points was measured with the inscribed timelines as a reference. This interval was measured on 8 beats at each cylinder pressure and the mean of these values was designated as the pulse transmission time. Using the distance between the strain gauges, the pulse wave velocity (PWV) between the brachial artery and radial artery loci was calculated. Wave velocities were then converted to volume distensibility (VD) using a modification of the Bramwell-Hill equation:24

\[
VD = \left(\frac{3.57}{PWV}\right)^2
\]  

Arterial blood pressure was measured during the recording of the arterial pulses at each cylinder pressure with an external cuff on the left arm and the Arteriosonde device (Model 1225, Roche Medical Electronics, Cranbury, New Jersey). The mean arterial pressure was calculated as one-third the pulse pressure plus the diastolic pressure, and transmural arterial pressure (TMP) was calculated by adding or subtracting the cylinder pressure from the mean arterial pressure. Plots of calculated VD and log VD vs TMP were then constructed for each patient.

We compared 57 mean blood pressure values, calculated from systolic and diastolic Arteriosonde cuff measurements, with simultaneously recorded and electronically damped intraarterial pulses in 20 other patients. The range of intraarterial mean pressure was from 85 to 126 mm Hg. There was no significant difference between the mean values (intraarterial 105.5 mm Hg vs cuff 103.8 mm Hg). The regression coefficient for the relationship was + 0.91 with a y intercept of 7.4 mm Hg and a standard error of estimate of ± 9.1 mm Hg. The electronically damped mean pressures taken from direct records of the arterial pulse are better estimates of true mean pressures than the values calculated from cuff data, but are not as accurate as values obtainable by integration of the direct pulse trace. The electronically damped mean pressures are advantageous, however, since they can be readily averaged over several respiratory cycles.

In six patients, the brachial and radial artery curves at each transmural pressure were also recorded on analog tape (Hewlett-Packard Company, B914C tape system). Five pulses at each cylinder pressure were then digitized and subjected to Fourier analysis. The average wave velocity of each of 10
harmonics was calculated and plotted against the harmonic for every transmural pressure. Using empiric curve fitting techniques, this family of curves was best approximated by the equation:

\[ y = a + \frac{b}{x} \]  

(2)

By using the regression curve for this equation, the characteristic wave velocity was defined as the average wave velocity of every harmonic above the point at which the succeeding wave velocity differed by less than 30%. This empirically defined characteristic wave velocity was then compared with the data obtained for the same beats in these 6 patients using the hand method of measurement.

Results

As expected, the relationship between VD and TMP was curvilinear (Figure 1). When log VD was plotted against TMP, the relationship was straightened in some patients (Figure 2) but not in others (Figure 3). Therefore, linear regression lines using the method of least squares were calculated for the lower TMP and upper TMP portions of the log VD-TMP plots using ambient mean blood pressure as the separation between upper and lower portions of the plot.

Using the obtained upper and lower slope regressions for all subjects, we calculated the volume dis-

Figure 1. Plot of transmural arterial pressure vs calculated volume distensibility in a single study.

Figure 2. Plot of transmural arterial pressure vs calculated log volume distensibility (VD) in a single study which shows a linear relationship. Least squares regression line.

Figure 3. Plot of transmural arterial pressure vs calculated log volume distensibility (VD) in a single study which shows a curvilinear relationship. Least squares linear regression.
tensibility at a variety of transmural pressures for each patient irrespective of his or her ambient blood pressure. A significant relationship was found between regressed volume distensibility and age at transmural pressures of 40, 60 and 90 mm Hg (Figures 4, 5, 6) but not at 120 or 150 mm Hg. These findings indicate that at ambient and lower transmural pressures, arterial distensibility increases with advancing age. No significant relationship between age and upper slope, lower slope, overall slope, or differences in slope could be obtained.

A representative plot of computer-generated wave velocity for each of the first 10 harmonics at three transmural pressures is shown in Figure 7. At ambient TMP, wave velocities are greater at lower harmonics. This curve shape is accentuated at higher TMP and attenuated at lower TMP. This observation also illustrates the need for a definition of characteristic wave velocity which takes into account different curve shapes at different transmural pressures. In the six patients whose curves were recorded on analog tape and similarly subjected to Fourier analysis, there were 73 comparisons between the computer-calculated average characteristic wave velocity for a given TMP and the average hand measurement for the same run. This relationship is shown in Figure 8 and has a regression coefficient of +0.97 and a y intercept near zero.

Figure 4. Scatterplot of age vs log volume distensibility (VD) at transmural pressure 40 mm Hg in 48 asymptomatic individuals. Linear regression using method of least squares.

Figure 5. Scatterplot of age vs log volume distensibility (VD) at transmural pressure 60 mm Hg in 48 asymptomatic individuals. Linear regression using method of least squares.

Figure 6. Scatterplot of age vs log volume distensibility (VD) at transmural pressure 90 mm Hg in 48 asymptomatic individuals. Linear regression using method of least squares.
Discussion

Although it is an important factor in circulatory physiology, arterial distensibility has been a difficult property to measure in intact humans. The measurement of arterial diameters using echo-ranging devices has been published but with conflicting results probably due to the study of different arteries and differences in technique. Arterial capacitance has been calculated from the diastolic portion of the brachial artery pulse tracing by considering it to be a monoexponential function. This technique is a simplification of a more complex mathematical model which considers the arterial tree in the time domain. This method, as well as the others, do not control blood pressure as a variable, and cannot distinguish between the loss of arterial distensibility due to high intraarterial pressure and loss of arterial distensibility due to intrinsic changes in the arterial wall. Simon and Safar have apparently replaced their monoexponential method with a newer technique using a pulsed Doppler velocimeter, an adjustable range-gated time system, and a double transducer probe. This technology has enabled them to measure brachial artery diameters in normal subjects, and in patients with hypertension, and to study the effect of nitroglycerin, but it has not been used in the calculation of arterial distensibility. Measurement of aortic input impedance is well described but is not readily applicable to large numbers of patients or to normal subjects who do not require catheterization of the ascending aorta. Therefore, there is no standard method against which any new technique can be compared for the estimation of arterial distensibility in normal individuals.

A new method to study arterial distensibility must have acceptable assumptions and be validated by testing it in a variety of circumstances to determine if the data generated is meaningful. The present method assumes that VD calculated from PWV data offers usable information in the description of arterial stiffness. The Bramwell-Hill equation, a simplification of the Moens-Korteweg relationship, assumes the density of blood to be constant and expresses pressure in mm Hg and wave velocity in meters/second. This equation describes wave travel in nonviscous, thin-walled tubes. The error introduced by this assumption appears acceptable since previous studies that compare measured arterial distensibility with that calculated from wave velocity data, have shown considerable scatter, but good agreement of mean values for a given vessel. These comparisons, together with the fact that our measured path length is short and relatively straight, suggest that the use of the Bramwell-Hill equation is satisfactory for our purposes. Our technique further assumes faithful transmission of altered cylinder pressure to the forearm arteries under study. This assumption has also been tested and found satisfactory. Although pressure changes within a water-filled plethysmograph are not faithfully transmitted to
all depths of the forearm, uniform transmission of such pressure changes in an air-filled plethysmograph has been demonstrated. Our control of blood pressure as a variable is of major importance in measurements of distensibility, since VD is highly dependent on TMP (Figures 1 to 3). The pulse wave velocity technique described here has already been used to demonstrate the similarity in the distensibility of forearm arteries between normal subjects and patients with essential hypertension when the differences in arterial pressure have been eliminated as a variable. This technique therefore indicates, in the forearm, that the increased arterial stiffness of hypertension is an effect rather than a cause. The method would also permit similar comparisons in the same individual before and after any therapeutic intervention which changes the blood pressure.

The data presented here show considerable variability in a group of normal subjects of widely disparate age. This variability is not unusual in studies of arterial distensibility and is due in part to the assumptions indicated above, to errors in the measurement of arterial path length, to undetected atherosclerosis (rare in forearm arteries) and to unmeasured variations between individuals in arterial diameters. Variability could also be due to subclinical disease in some of the asymptomatic population studied, and to true variations in arterial distensibility among normal persons. Factors that contribute little to the scatter of the data include differences in flow rate through the arteries, small differences in mean blood pressure in the two arms, minor variations in blood viscosity between persons, and level of the mean arterial pressure, control of which was described earlier.

In the present study, increased compliance could be demonstrated at lower transmural pressures with increasing age but no change in stiffness could be demonstrated at higher pressures. It may be that because of the shape of the VD-TMP plot (Figure 1), the small changes in volume distensibility which occur with increasing pressures are difficult to detect. Conversely, the large changes in volume distensibility with lower than ambient TMP are more readily measured.

Our finding of increasing arterial distensibility with advancing age is contrary to common belief. Early data by Bramwell et al. confirmed by Fulton and McSwiney indicated that pulse wave velocity (and thus arterial stiffness) increased with aging. These investigators calculated the differences in arrival times between the carotid and brachial or radial pulses and used the position of the sternoclavicular joint to divide the arterial path length into carotid and subclavian portions. One distance was then subtracted from the other to calculate path length. The measurement inaccuracy was compounded by the assumption that wave velocity was equal in the carotid and subclavian system. The most important objection to these early studies, however, is the lack of control of blood pressure as a variable. The known tendency for blood pressure to rise with increasing age could also explain their results. More recently, Gosling and King showed a relationship between blood pressure and wave velocity similar to ours using Doppler shifted ultrasound pulse detection in the arterial tree of the leg. At the same blood pressures, asymptomatic individuals ages 50 to 60 years had faster wave velocities than persons aged 20 to 50 years. These differences were small, and according to the authors, close to the resolution limit of the method. Confidence limits and statistical analyses were not provided.

Other in vitro and in vivo techniques have also been used to support the thesis of arterial stiffening with age. Histologic and chemical studies of arteries have shown changes in composition with aging which explain stiffening of the walls as a material. However, in a detailed and elegant study, Learoyd and Taylor have shown that arterial segments studied in vitro are returned to their original dimensions, dynamic arterial compliance is increased in older iliac and femoral vessels when compared to younger ones. Apparently, the reduction found in arterial diameter and increase in wall thickness more than offsets the effect of increased wall tension produced by a change in the wall composition. These data were interpreted as a general weakening of the arterial walls. Learoyd and Taylor also compared 10 directly measured PWV with wave velocities calculated from independently determined modulus measurements under approximately the same conditions. Mean values were roughly equivalent, with the usual large scatter. In the thoracic and abdominal aorta, measured and calculated waves traveled faster in “old” persons (over 35 years old) than in younger persons, but these differences were probably not significant. There was no difference in rate of wave travel in the iliac arteries studied, but the calculated wave velocity in the femoral arteries were slower in the “old” patients indicating greater distensibility.

The present study tends to confirm the findings of Learoyd and Taylor by demonstrating an increase in volume distensibility with advancing age in another muscular artery, the brachial. Since different parts of the arterial tree have very different wall properties (for example proximal vs distal aorta, carotid, coronary, femoral) the results obtained here cannot be extrapolated to the entire arterial tree or to any of its parts other than the brachial.

The close association between the hand method of pulse wave velocity measurement and the characteristic wave velocity obtained by Fourier analysis indicates that both techniques measure the same variable and that the hand method is, therefore, suitable for this purpose.

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