Carotid Artery Distensibility and Distending Pressure in Hypertensive Humans

Stéphane Laurent, Bernard Caviezel, Lionel Beck, Xavier Girerd, Eliane Billaud, Pierre Boutouyrie, Arnold Hoeks, Michel Safar

Abstract Whether the decrease in large-artery distensibility observed in hypertensive patients is due primarily to an increase in distending pressure or to hypertension-induced changes in structural properties has been much debated. We determined noninvasively the diameter-pressure curve of the common carotid artery over the systolic-diastolic range by continuously recording both the pulsatile changes in internal diameter (high-resolution echo-tracking system) and, simultaneously on the contralateral artery, the pressure waveform (high-fidelity applanation tonometry). We then derived the distensibility/pressure curve and compared arterial distensibility in 14 normotensive subjects and 15 age- and sex-matched hypertensive subjects at their respective mean arterial pressures (MAP) and at a common distending pressure: 100 mm Hg. Distensibility decreased as blood pressure increased, and distensibility at MAP was significantly lower in hypertensive than in normotensive subjects (7.8±0.7 versus 11.7±1.7 kPa·1·10⁻³, mean±SEM; P<.05). In hypertensive subjects, the distensibility-pressure curve was shifted toward higher levels of blood pressure, and a large part of the curve overlapped that of normotensive subjects. No significant downward shift of the distensibility-pressure curve was observed in hypertensive subjects, and distensibility at 100 mm Hg was not significantly different from that of normotensive subjects (10.0±1.0 versus 9.0±1.1 kPa·1·10⁻³). Distensibility at 100 mm Hg decreased with aging (P<.05) and was not reduced in hypertensive subjects compared with normotensive subjects after adjustment for age. These results suggest that the decrease in common carotid artery distensibility in hypertensive subjects is due primarily to the increased distending blood pressure and that age-independent structural modifications of the arterial wall play only a minor role. (Hypertension. 1994; 23[Part 2]:878-883.)

Key Words • carotid artery, common • hypertension, essential • ultrasonography • tonometry

In regard to the large artery, hypertension is often considered an accelerated form of aging, since pathological arterial wall changes similar to those of aging are seen at an earlier age. As in aging, the major changes in impedance and in arterial pressure and flow wave contours are due to decreased arterial distensibility. We have previously shown that local common carotid arterial distensibility and compliance decreased more rapidly with aging in hypertensive subjects than in normotensive subjects. Two different mechanisms have been suggested to explain these earlier alterations in hypertensive subjects: structural changes due to arterial degeneration or functional changes due to the increased distending pressure. Gribbin et al and Smulyan et al have shown, by enclosing the forearm inside an airtight box and varying transmural pressure, that the increased distending pressure alone may explain the higher pulse wave velocity of hypertensive subjects. In addition, arterial wall hypertrophy in hypertensive subjects is not necessarily associated with reduced distensibility. Indeed, we observed at the site of the radial artery that, despite wall hypertrophy, arterial distensibility and compliance in hypertensive patients were not significantly different from those of normotensive control subjects when the two populations were studied at their mean arterial pressure (MAP). Furthermore, when the two populations were compared at the same blood pressure level (ie, 100 mm Hg), distensibility (Dₘₐ) and compliance (Cₘₐ) in hypertensive subjects were not significantly lower than in normotensive subjects, being either unchanged or higher.

Our objective was therefore to determine, at the site of the larger, more proximal, and more elastic common carotid artery (CCA), whether the decrease in arterial distensibility observed in hypertensive patients (HT) was due primarily to an increase in distending pressure or to age-independent structural changes of the arterial wall.

Methods

Subjects and Patients

Fourteen normal subjects (NT) 24 to 72 years old (50±5 years, mean±SEM) and 15 untreated mild or moderate essential hypertensive patients 21 to 75 years old (51±3 years) were included in the study. Normotension was defined by auscultatory blood pressure values below 140/90 mm Hg at repeated visits. Hypertension was defined as mild to moderate by supine diastolic pressures of 95 to 114 mm Hg on three consecutive visits. No patient had hypertension complications, valvular heart disease, major arrhythmia, atherosclerotic carotid artery plaque, or diseases of noncardiovascular nature. To increase the likelihood of carotid artery wall hypertrophy in our hypertensive patients, we selected 11 patients with either never-treated sustained hypertension of long duration or cessation of treatment at least 6 months before the study. Four other patients had...
Morphometric and Hemodynamic Parameters of Normotensive Subjects and Hypertensive Patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normotensive Subjects</th>
<th>Hypertensive Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=14)</td>
<td>(n=15)</td>
</tr>
<tr>
<td>Age, y</td>
<td>50±5</td>
<td>51±3</td>
</tr>
<tr>
<td>Sex ratio, M/F</td>
<td>8/6</td>
<td>6/7</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23±1</td>
<td>26±1*</td>
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<tr>
<td>Total serum cholesterol, mmol/L</td>
<td>5.5±0.4</td>
<td>5.7±0.3</td>
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<tr>
<td>Blood glucose, mmol/L</td>
<td>5.9±0.3</td>
<td>5.4±0.2</td>
</tr>
<tr>
<td>Smoker/nonsmoker</td>
<td>10/4</td>
<td>9/6</td>
</tr>
<tr>
<td>SAP, mm Hg</td>
<td>117.7±3.3</td>
<td>155.6±3.4†</td>
</tr>
<tr>
<td>DAP, mm Hg</td>
<td>71.4±2.7</td>
<td>93.3±1.6†</td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>86.3±2.4</td>
<td>114.8±2.1†</td>
</tr>
<tr>
<td>Hemodynamic parameters at MAP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dd, mm</td>
<td>6.87±0.18</td>
<td>7.34±0.25</td>
</tr>
<tr>
<td>Distensibility, kPa⁻¹·10⁻³</td>
<td>11.7±1.7</td>
<td>7.8±0.7*</td>
</tr>
<tr>
<td>Compliance, m²·kPa⁻¹·10⁻⁷</td>
<td>8.72±1.0</td>
<td>6.31±0.9*</td>
</tr>
<tr>
<td>Hemodynamic parameters at 100 mm Hg</td>
<td></td>
<td></td>
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<tr>
<td>Dd, mm</td>
<td>7.23±0.16</td>
<td>7.45±0.25</td>
</tr>
<tr>
<td>Distensibility, kPa⁻¹·10⁻³</td>
<td>9.0±1.1</td>
<td>10.0±1.0</td>
</tr>
<tr>
<td>Compliance, m²·kPa⁻¹·10⁻⁷</td>
<td>6.9±0.9</td>
<td>7.8±1.1</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; and Dd, end-diastolic internal diameter. Smoker/nonsmoker: Subjects were classified as smokers if they smoked at least one cigarette per day and as nonsmokers if they had never smoked or had stopped smoking at the time of the examination. Values are mean±SEM.

*P<.05; †P<.001.

The study was approved by the Ethics Committee of the Broussais Hospital, and all patients gave written informed consent. The principal clinical characteristics of the subjects and patients are given in the Table.

The investigation was performed between 9 and 11 AM in a controlled environment kept at 22±2°C. Blood pressure was measured with a mercury sphygmomanometer and a cuff adapted to arm circumference after the subjects had been recumbent for at least 15 minutes. The diameter-pressure curve of the CCA was then determined noninvasively by simultaneous and continuous recording of the systolic-diastolic changes in internal diameter and pressure.

Measurement of Pulsatile Changes in CCA Diameter

Vessel wall motion of the right CCA was measured with an original pulsed ultrasound echo-tracking system based on Doppler shift. The operating frequency of the device was 5 MHz. The details of this method have been described elsewhere. Briefly, this system allows the transcutaneous assessment of arterial wall displacement during the cardiac cycle and, hence, of the time-dependent changes in arterial diameter relative to initial diameter at the start of the cardiac cycle. The radio frequency signal of four to eight cardiac cycles was recorded, digitized, and temporarily stored in a large memory. Two sample volumes selected under cursor control were positioned on the anterior and posterior arterial walls. To overcome the possibility that nearby structures generating prominent echoes might temporarily enter the selected sample volumes, thus obscuring the vessel wall signal, a tracking system was developed and allowed the vessel walls to be tracked by the sample volumes. Arterial wall displacement was then obtained by processing the Doppler signals originating from the two selected sample volumes. A typical displacement waveform of the anterior and posterior walls of the CCA is shown in Fig 1. The echo-tracking system computed the successive values of internal end-diastolic diameter and stroke change in diameter and digitized the displacement waveform.

Fig 1. Typical simultaneous recording of diameter changes and pressure waveforms at the sites of the right and left common carotid artery, respectively.
Measurement of Pulsatile Changes in CCA Pressure

The left common carotid arterial pressure wave contour was recorded noninvasively according to methodology previously validated and published by others. Briefly, we used a pencil-type probe incorporating a high-fidelity strain-gauge transducer (Millar Instruments Inc). The transducer has a small pressure-sensitive area (0.5x1.0 mm) with a frequency response >2 kHz that is planar with a larger area (7-mm diameter) of flat surface that is in contact with the skin overlying the pulse. The tonometer is internally calibrated (1 mV=1 mm Hg) with a conventional Millar preamplifier (TCB-500). Waveforms were simultaneously recorded on a Gould 8188 recorder (Gould Electronics) at 100 or 200 ms and computerized by the echotracking system.

This instrument is based on the principles of applanation tonometry as used in ocular tonometry for measuring intracocular pressure. In theory, application of a curved surface of a pressure-containing structure equalizes the circumferential stress of the structure's wall and allows the sensor to measure true intra-arterial pressure. The accuracy of the probe has been validated in humans. Noninvasively measured carotid pulse contours and invasively measured ascending aortic pulses have been shown to have close similarities in both time and frequency domains. We have previously reported, in 16 subjects undergoing cardiac catheterization for suspected coronary artery disease, a significant positive correlation (r=.92; P<.0001) between the CCA pressure pulse measured locally with tonometry and the aortic arch pulse pressure measured invasively. In another study in 105 subjects, brachial pulse pressure measured by conventional sphygmomanometry was strongly correlated with radial pulse pressure measured by applanation tonometry (r=.97; slope, 0.98; intercept, 1.4 mm Hg).

Determination of the Cross Section–Pressure Curve

The cross section–pressure curve was derived from the two simultaneous and continuous recordings of arterial diameter and pressure waveforms, each performed by an experienced investigator. Since pulse pressure measurement with applanation tonometry requires a hold-down pressure but diameter measurement does not, applanation tonometry was performed on one side and echotracking on the other. Arbitrarily, applanation tonometry was performed on the left CCA and echotracking on the right. We previously reported that the side of measurement did not influence arterial dimensional data. We checked that the hold-down pressure of the tonometer did not influence contralateral carotid internal diameter. We also checked that the pressure waveform was not significantly different whether measured in the right or left CCA. Since applanation tonometry is calibrated to provide absolute pressure changes but not the absolute level of instantaneous blood pressure, we first had to determine the absolute values of the 512 different points of the digitized pressure waveform. This was done by the following procedure. Systolic and diastolic blood pressures were measured in both arms and checked to be equal at both sites. MAP was calculated according to the usual definition: diastolic blood pressure plus one third of the pulse pressure. We set the carotid MAP derived from the area under the curve (AUC) of the CCA pressure waveform equal to the brachial MAP. The absolute values of the different points of the pressure waveform were then calculated. The simultaneity of diameter- and pressure-waveform events was guaranteed by an ECG trigger.

The relation between the pressure P and the cross section S was determined over the systolic-diastolic range and fitted with the model of Langewouters et al using an arctangent function and three optimal fit parameters, as already described.

\[
S = \frac{\pi}{2} \tan^{-1}\left(\frac{(P-B)\gamma}{\alpha}\right)
\]

where \(S = \pi D^2/4\) and D is the internal diameter, assuming a cylindrical vessel. The three parameters \(\alpha, \beta,\) and \(\gamma\) fully characterize the diameter-pressure curve. Arterial cross-sectional compliance (C), in the case of a cylindrical vessel, is defined by the change in luminal cross-sectional area (\(\Delta S\)) for a given change in intravascular pressure (\(\Delta P\)), ie, \(C=\Delta S/\Delta P\). Because of the nonlinearity of the cross section–pressure curve, compliance decreases as blood pressure increases. To determine compliance for a given level of blood pressure, we established the compliance-pressure curve over the systolic-diastolic range. This was done by deriving the equation of the cross section–pressure curve. By use of Equation 1, the following analytical form was obtained for the local arterial compliance:

\[
\frac{1}{C} = \frac{\gamma}{1 + ((P-B)/(\alpha))^{\gamma}}
\]

Arterial cross-sectional distensibility (Dist) is the compliance value normalized for the luminal cross-sectional area and is defined by \(\text{Dist}=((1/S)\times(\Delta S/\Delta P))\). From Equation 1, the following analytical form was obtained for the local arterial distensibility:

\[
\text{Dist} = \frac{1}{S} = \frac{\alpha}{\gamma} \left(\frac{1}{1 + ((P-B)/(\alpha))^{\gamma}}\right)
\]

Compliance and distensibility were calculated at the respective MAP of HT and NT (\(C_{\text{MAP, HT}}\) and \(C_{\text{MAP, NT}}\)) and at 100 mm Hg, a value common to all patients (\(C_{100, HT}\) and \(C_{100, NT}\)). In the present study, we assessed the elastic response of the artery as a hollow structure through distensibility- and compliance-pressure curves. We did not intend to determine the elastic properties of the wall material, which requires the measurement of arterial wall thickness to calculate the incremental modulus of elasticity or Young's modulus.

Repeatability of Measurements

Repeatability of CCA diameter and pulse pressure measurements and of \(C_{\text{MAP, HT}}, C_{\text{MAP, NT}}, \text{Dist}_{\text{MAP, HT}},\) and \(\text{Dist}_{\text{MAP, NT}}\) determinations was investigated in five subjects through calculation of the repeatability coefficient (RC) as defined by the British Standard Institution, ie, according to the formula

\[
\text{RC} = \frac{\Sigma D i}{N}
\]

where N is the sample size and Di the relative difference within each pair of measures. This coefficient is the standard deviation of the estimated difference between two repeated measurements. RCs for intraobserver repeatability (comparison of two determinations obtained at intervals of 1 month by the same observers) were as follows: CCA internal diameter, 0.423 mm; pulse pressure, 6.8 mm Hg; \(C_{\text{MAP, HT}}\), 0.82 m²·kPa⁻¹·10⁻⁷; \(C_{\text{MAP, NT}}\), 0.68 m²·kPa⁻¹·10⁻⁷; \(\text{Dist}_{\text{MAP, HT}}\), 4.7 kPa⁻¹·10⁻⁷; and \(\text{Dist}_{\text{MAP, NT}}\), 3.12 kPa⁻¹·10⁻⁷.

Statistical Analysis

All values were averaged and expressed as mean±SEM. Blood pressure and arterial parameters were compared in NT and HT by an unpaired Student's t test. To compare distensibility at the same blood pressure level in HT and NT, respective values of \(\text{Dist}_{100, HT}\) were compared and a significant downward (or upward) shift of the distensibility-pressure curve of HT was sought. The latter procedure was initiated by calculating, for each subject, the AUC of his or her distensibility-pressure curve corresponding to the overlap between the
Results

The two groups were comparable as far as total serum cholesterol, blood glucose, and smoking were concerned (Table). Compared with NT, the diameter-pressure curve of HT was shifted toward higher levels of blood pressure, but no significant upward shift was observed (Fig 2A). Compared with NT, the compliance-diameter curve of HT was shifted toward higher levels of diameter (Fig 2B).

Distensibility decreased as blood pressure increased (Fig 3). In HT, Dist$_{\text{MAP}}$ was significantly reduced compared with NT (Fig 3 and Table). In HT, although the distensibility-pressure curve was shifted toward higher levels of blood pressure, a large part of it still overlapped that of NT. No significant downward or upward shift was observed in HT, and for a given level of blood pressure, distensibility was not significantly different between HT and NT (Table). Similar results were observed when compliance-pressure curves were compared between HT and NT.

Two main factors influenced the decreases in distensibility ($\text{Dist}_{\text{MAP}}$) and compliance ($\text{C}_{\text{MAP}}$): aging ($P<.001$ and $P<.05$, respectively) and obviously the increase in resting MAP ($P<.01$ and $P<.001$, respectively). $\text{C}_{\text{MAP}}$ but not $\text{Dist}_{\text{MAP}}$ decreased with aging ($P<.05$). Although mean ages were not significantly different between NT and HT, the age range was wide inside each group (24 to 72 years in NT and 21 to 75 years in HT). To take this
characteristic into account, Dist$_{100}$ was correlated both to the age of each subject or patient and to his or her status (NT or HT). Age-adjusted Dist$_{100}$ was not significantly reduced in HT compared with NT.

**Discussion**

This study, designed to evaluate the elastic properties of the CCA through its distensibility- and compliance-pressure curves, provides the first noninvasive evaluation of the CCA pressure-diameter curve in hypertensive patients. The main finding is that, at a given blood pressure level common to both groups, CCA distensibility was not reduced in hypertensive patients compared with that in age- and sex-matched normotensive subjects.

**Consideration of Methods**

Both completely noninvasive methods used in this study (applanation tonometry and echo-tracking system) have been validated previously. In contrast to pulse pressure, which has a smaller pulse amplitude in central than in peripheral arteries, mean blood pressure does not vary significantly between central and peripheral sites, allowing carotid MAP to be set equal to brachial MAP.

To compare distensibility at the same blood pressure level in HT and NT, the distensibility-pressure curves were compared both at the arbitrarily chosen common level of 100 mm Hg and within the range of pulse pressure common to both groups. We preferred to calculate the distensibility-pressure curve over the systolic-diastolic range rather than calculating $C_{MAP}$ and $D_{MAP}$ from the end points of the pressure-diameter curve at different MAP levels. Indeed, the diameter-pressure curve can be affected by the maneuvers used to vary blood pressure, particularly through changes in baroreflex activity and CCA vasomotor tone.

We should mention the possibility that with such small numbers of patients, there really are differences in diameter between the two groups but that statistical differences are not achieved because of large standard errors (type II statistical error). With the nonparametric Mann-Whitney $U$ test, there was a tendency for a statistical significance ($P = .12$) when diameter was compared at respective MAP between HT and NT. However, diameter at 100 mm Hg was not significantly different ($P = .48$) between HT and NT. Further studies including a larger number of patients should be performed to demonstrate unequivocally an upward shift of the diameter-pressure curve in HT.

Our repeatability results indicate that distensibility and compliance measurements can be used for cross-sectional clinical studies provided that they are performed by two experienced investigators, following a standardized protocol. For example, the probability of two $C_{100}$ values differing by more than 1.33 (1.96 times 0.68) m$^2$·kPa$^{-1}$·10$^{-7}$, based on measurements performed by the same observers using the previously described methodology, is only 5%.

**Interpretation of the Findings**

That similar distensibility and compliance values were observed in hypertensive and normotensive subjects when the two groups were studied at the same blood pressure level suggests that the increase in distending pressure per se could explain the decrease in arterial distensibility and compliance observed in HT. Other studies on forearm arterial distensibility in hypertension reached the same conclusions. Using determinations of pulse-wave velocity measured on the human forearm enclosed in an airtight box, Gribbin et al. showed that, for the same mean transmural pressure, NT and HT had the same pulse-wave velocity and therefore the same distensibility as derived from the Bramwell and Hill formula. However, arterial diameter and volume were not measured in these studies. In the present study, the shift of the compliance-diameter curve of HT toward higher levels of diameter suggests that the decreased compliance seen in HT may be due to both increased pressure and diameter.

By carefully selecting a majority of hypertensive patients who either had never-treated, sustained hypertension of long duration or had stopped treatment at least 6 months before the study, we increased the likelihood of carotid artery wall structural changes being present in our population. We must admit that we cannot rule out the possibility that the never-treated hypertensive subjects may not have been hypertensive long enough for the wall to have undergone histological and mechanical changes such as seen in experiments on spontaneously hypertensive rats. However, since it is likely that structural changes of the carotid artery wall were present in our hypertensive patients, the present results suggest that hypertension-induced changes in CCA structural properties probably play only a minor role in the observed decrease in distensibility and compliance. In addition, from the present data and the values of common carotid artery wall thickness observed in normotensive and hypertensive subjects by Roman et al., it can be estimated that Young's modulus (i.e., the elastic properties of the wall material) was not significantly different between NT and HT when the two populations were compared at their respective MAPs. Our results on CCA distensibility are in contrast to aging-induced changes in CCA properties. Indeed, aging may alter CCA distensibility independently of distending blood pressure, since we observed a negative correlation between Dist$_{100}$ and age. Several authors have shown that hypertension-induced changes in structural properties of the carotid artery wall may be due to both increased pressure and diameter rather than through hypertension-induced changes in structural properties of the CCA.

**References**


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