Conduit Artery Compliance and Distensibility Are Not Necessarily Reduced in Hypertension

Daniel Hayoz, Blaise Rutschmann, François Perret, Michel Niederberger, Yanik Tardy, Vincent Mooser, Jürg Nussberger, Bernard Waerber, and Hans R. Brunner

The goal of this study was to investigate whether the elastic behavior of conduit arteries of humans or rats is altered as a result of concomitant hypertension. Forearm arterial cross-sectional compliance-pressure curves were determined noninvasively by means of a high precision ultrasonic echo-tracking device coupled to a photoplethysmograph (Finapres system) allowing simultaneous arterial diameter and finger blood pressure monitoring. Seventeen newly diagnosed hypertensive patients with a humeral blood pressure of $163/103 ± 4.4/2.2$ mm Hg (mean±SEM) and 17 age- and sex-matched normotensive controls with a humeral blood pressure of $121/77 ± 3.2/1.9$ mm Hg were included in the study. Compliance-pressure curves were also established at the carotid artery of 16-week-old anesthetized spontaneously hypertensive rats ($n = 14$) as well as Wistar-Kyoto normotensive animals ($n = 15$) using the same echo-tracking device. In these animals, intra-arterial pressure was monitored in the contralateral carotid artery. Mean blood pressures averaged $197 ± 4$ and $140 ± 3$ mm Hg in the hypertensive and normotensive rats, respectively. Despite the considerable differences in blood pressure, the diameter-pressure and cross-sectional compliance-pressure and distensibility-pressure curves were not different when hypertensive patients or animals were compared with their respective controls. These results suggest that the elastic behavior of a medium size muscular artery (radial) in humans and of an elastic artery (carotid) in rats is not necessarily altered by an increase in blood pressure.

KEY WORDS • elasticity • arteries • essential hypertension • ultrasonography • spontaneously hypertensive rats

The structural changes of arterial wall observed in hypertensive patients may reflect either a primary defect or a consequence of an elevated blood pressure. Increased vascular thickness is thought to be a key determinant of the mechanical behavior of conduit vessels. Several physical parameters have been used in an attempt to assess the influence of morphological changes on arterial impedance. Pulse wave velocity per sec or in combination with mean arterial diameter measurements, arterial stiffness, exponential diastolic pressure wave decay analysis, and invasive compliance recordings are among the approaches used to characterize the mechanical properties of the arterial wall associated with hypertension. Arterial compliance, which can be defined as the blood volume stored or released given a specific change in intraluminal blood pressure, as well as the cross-section adjusted distensibility, decreases in close relation with blood pressure when this latter increases. Because the pressure-volume relation is clearly non-linear, compliance changes dramatically with variations in blood pressure. Therefore, pressure has to be accounted for as a variable. This has not always been possible in the past due to methodological difficulties. In the present study, variations in the internal diameter of the radial artery and in finger blood pressure were recorded simultaneously and continuously by means of a noninvasive, high-precision echo-tracking device coupled to a commercially available photoplethysmograph. Seventeen newly diagnosed hypertensive patients and an equal number of sex- and age-matched normotensive subjects were investigated. Additional measurements were performed in anesthetized spontaneously hypertensive rats (SHR) and normotensive Wistar-Kyoto (WKY) control rats. In these animals, the internal diameter of the external carotid artery was tracked using the same device, and intra-arterial blood pressure was monitored via a catheter placed in the contralateral carotid artery.

Methods

Human Studies

Seventeen newly diagnosed and untreated hypertensive patients (office blood pressure was more than 160 mm Hg or diastolic blood pressure more than 95 mm Hg, or both, on at least three occasions) and 17 normotensive subjects were included in the current study. The protocol for this study was approved by the institutional ethics committee. Informed consent was obtained from all participants for entry into the study.
Table 1. Characteristics of the Human Study Groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normotensive (n=17)</th>
<th>Hypertensive (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (F/M)</td>
<td>7/10</td>
<td>7/10</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>47.5 (23–65)</td>
<td>49.7 (24–67)</td>
</tr>
<tr>
<td>Office humeral blood pressure (mm Hg)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>121±3.2</td>
<td>163±4.4†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>77±1.9</td>
<td>103±2.2†</td>
</tr>
<tr>
<td>Finger blood pressure (mm Hg)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>121±5.2</td>
<td>148±4.2†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>68±2.1</td>
<td>82±2.6†</td>
</tr>
<tr>
<td>Internal diameter of radial artery (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>2.807±0.134</td>
<td>2.866±0.081</td>
</tr>
<tr>
<td>Diastolic</td>
<td>2.767±0.133</td>
<td>2.830±0.081</td>
</tr>
<tr>
<td>Plasma cholesterol (mmol/l)</td>
<td>4.45±0.16</td>
<td>5.60±0.27†</td>
</tr>
<tr>
<td>Smokers (No.)</td>
<td>8</td>
<td>11</td>
</tr>
</tbody>
</table>

Values are mean±SEM.*Blood pressure was measured with different techniques on different days: office humeral blood pressure was measured with subject in seated position, and finger blood pressure was measured after the subject had been in the supine position for 15 minutes. †p<0.01 vs. normotensive group.

The two groups were age- and sex-matched. Secondary hypertension was excluded on the basis of medical history, physical examination, and laboratory tests. The control group consisted of normotensive subjects recruited from the medical, nursing, and technical hospital staff. The clinical characteristics of both study groups are presented in Table 1.

Technique of Arterial Diameter and Pressure Measurement

All subjects were studied in supine position after 15 minutes of rest in a room with a constant temperature of 23°C. Arterial measurements were carried out on the right radial artery. For this purpose the right supinated arm was placed in a gutter to avoid involuntary movements. The measurements were always performed at the same time of the day by a single operator. The description of the measuring device as well as preliminary observations made in humans using this new system have been reported previously.18,19 Briefly, the apparatus consists of an A-Mode, ultrasonic echo-tracking device that measures internal radial artery diameter variations with a precision close to 1 μm. The degree of resolution is made possible by oversampling (5,000 arterial diameter measurements per second) and averaging 16 consecutive values. For the recordings, a 10-MHz probe is positioned perpendicularly over the artery without direct contact with the skin. The Doppler technique is used for guidance of the probe and an ultrasonic gel is used for signal transduction.

In the present study, measurements were obtained at three different locations evenly spaced (2 cm) along the radial artery starting from the wrist. Five arterial recordings were performed at each position, the whole procedure being accomplished within a 15-minute period. The cross-sectional compliance–pressure (C–P) curves obtained at these three different positions along the radial artery axis were averaged for each subject. This latter C–P relation was used for calculating the mean C–P curve for the different study groups. In each group, the mean of systolic and diastolic pressure was taken as cut point for the upper and lower limit of the curves. The backscattered echoes from inner walls are visualized on an oscilloscope and a Polaroid picture of the analog display is taken for the record. The ultrasound device is coupled to a photoplethysmograph (Finapres system, Ohmeda, BOC Group Inc., Englewood, Colo.), which measures blood pressure continuously and noninvasively at the middle finger. This latter instrument based on a volume-clamp method has been shown previously to provide accurate blood pressure measurements as compared with blood pressure measured intra-arterially.20–24 The simultaneous and continuous acquisitions of internal arterial diameter and blood pressure (Figure 1A) are processed on line to compute a cross-section–pressure relation (Figure 1B). This latter is subsequently converted into a compliance–pressure curve (Figure 1C), which is fully characterized over the whole range of blood pressure. This curve fits best with an arctangent function described by Lang-
Table 2. Characteristics of the Rats

<table>
<thead>
<tr>
<th>Variables</th>
<th>WKY (n=15)</th>
<th>SHR (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td>325±3</td>
<td>327±6</td>
</tr>
<tr>
<td>Blood pressure during anesthesia (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>131±3</td>
<td>192±1*</td>
</tr>
<tr>
<td>Diastolic</td>
<td>88±3</td>
<td>133±2*</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>431±10</td>
<td>405±14</td>
</tr>
<tr>
<td>Internal diameter of carotid artery (mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>1.195±0.06</td>
<td>1.304±0.10</td>
</tr>
<tr>
<td>Diastolic</td>
<td>1.037±0.05</td>
<td>1.190±0.10</td>
</tr>
</tbody>
</table>

Values are mean±SEM. WKY, Wistar-Kyoto rats; SHR, spontaneously hypertensive rats; bpm, beats per minute. *p<0.01 vs. WKY rats.

eewouters et al. Cross-sectional compliance (C) in the case of a cylindrical vessel is given by

$$C = \frac{\delta s}{\delta p}$$

where $\delta s$ is change in cross-section and $\delta p$ is change in blood pressure. Arterial cross-sectional distensibility (D) is the inverse of the Peterson elastic modulus, i.e., the compliance value normalized for the cross-section ($s$). It is defined by

$$D = \frac{1}{s} \cdot \frac{(\delta s)}{(\delta p)}$$

Animal Experiments

Fifteen 16-week-old normotensive male WKY rats and 14 age- and sex-matched SHR were obtained from IFFA-CREDO, Lyon, France. They were housed in a room at a constant temperature of 23°C. Ordinary rat chow (UAR, A04, Villeremoison-sur-Orge, France) containing 100 μmol sodium per gram and tap water were given ad libitum. On the day of the experiment, anesthesia was induced with ether and then maintained with fluorthane at a concentration of 1.5%. The left external carotid artery was cannulated with a catheter (PE-50) filled with a heparinized 0.9% NaCl solution. Intraarterial pressure and heart rate were monitored as described previously using a computerized data acquisition system. The internal diameter of the right external carotid artery was measured at the same time using our new ultrasonic device. The whole procedure lasted 15–20 minutes. The different curves were established over the range of pressures actually measured in the two groups of rats, the mean diastolic and systolic values serving as lower and upper limits. The characteristics of the two groups of animals are summarized in Table 2.

Statistical Analysis

Student's t test for unpaired data was used to compare the general baseline characteristics of the two clinical and experimental groups. Differences were considered significant for values of $p<0.05$. Data are reported as mean±SEM. Statistical analysis of compliance-pressure and distensibility-pressure curves obtained in humans were done using a multivariate analysis based on Hotelling's $T^2$ considering compliance values at three arbitrary defined blood pressures in the proximity of measured values (80, 100, and 120 mm Hg).

Human Studies

Figure 2 depicts the diameter–pressure curves established in the hypertensive patients and the normotensive subjects. There was a more than 5 mm Hg overlap between the finger pressures measured in the two groups. The internal diameter of the radial artery increased in parallel with blood pressure and tended to be larger in hypertensive patients than in normotensive subjects (Table 1). Due to the widespread distribution of this parameter, however, no significant difference was observed between the two study populations. There was no relation between age and arterial diameter.

The compliance–pressure curves are shown in Figure 3 (upper panel). The behavior of the arterial wall was very similar in the two groups. No significant difference in cross-sectional arterial compliance was found between
hypertensive patients and normotensive subjects. Actually, there was a considerable scatter of individual compliance–pressure curves in each group. This is illustrated by the cross-sectional compliance values measured in each hypertensive patient and normotensive subject at pressures of 100 and 120 mm Hg, i.e., at pressures common to both populations (Figure 4). Similarly, there was no difference in the cross-sectional distensibility–pressure curves between the two groups (Figure 3, lower panel). The stiffness index \( \beta \) defined by Kawasaki et al.\(^9\), which compensates for the nonlinear relation between the elastic modulus and the diameter, was also comparable in hypertensive patients (42.89±6.94) and normotensive subjects (40.37±3.10).

**Animal Experiments**

Because the SHR exhibited quite severe hypertension, their pressures hardly overlapped with those of normotensive rats (Table 2). Figure 5 illustrates the diameter–pressure relations determined in the two groups of animals. The curve obtained in hypertensive rats appeared to be the direct continuation of that established in normotensive animals. Figure 6 depicts the compliance– and distensibility–pressure curves. There exists a slight difference between hypertensive and normotensive animals in the small range of near overlapping pressures. If anything, cross-sectional arterial compliance and distensibility are higher in SHR than in WKY rats.

**Discussion**

In the present study, cross-sectional compliance of the radial artery was measured noninvasively in newly diagnosed, untreated hypertensive patients and age- and sex-matched normotensive control subjects. The measured compliance could be related to the simultaneously determined finger blood pressure using a recently developed technique. The hypertensive patients exhibited a forearm arterial cross-sectional compliance–pressure curve similar to that of the normotensive control subjects. The same was true for the carotid artery diameter–pressure relation established in hypertensive rats, which did not differ from that observed in normotensive controls. In this latter experiment, diameter and blood pressure variations were both recorded at the carotid arteries, thus eliminating the need for correction of the diameter–pressure curve phase shift, which we face in the clinical situation because the sites for arterial diameter and blood pressure measurements differ.\(^8\)

The present data obtained in humans as well as in rats confirm the nonlinear internal diameter–pressure relation (and thus nonlinear cross-sectional compliance– and distensibility–pressure relation) that has been described previously for various muscular and elastic arteries.\(^14-16\) The results demonstrate a considerable scatter of individual compliance–pressure curves in the normal and the hypertensive subjects. The radial artery is a medium-sized muscular artery. This is important since the physical characteristics of the arterial wall in predominantly muscular arteries have been shown to be much more variable than in elastic arteries because of a
greater influence of vasoactive stimuli.9 Arteries with less physiological variability of the mechanical characteristics might exhibit more important changes resulting from modifications of their environment such as hypertension or drug-related modifications. For this reason and because of their major clinical implications, elastic arteries with a smaller quantity of smooth muscle cells, e.g., carotid and femoral arteries, could appear more appropriate candidates. At present, in human subjects there is yet a strong limitation to continuous and accurate noninvasive monitoring of blood pressure in these arteries.

When compared at their respective different mean arterial blood pressures, hypertensive patients exhibit a lower arterial compliance than normotensive control subjects. This is inherent to the compliance-pressure relation, as shown in Figure 1C, with increasing pressure compliance decreases or, in other words, the arterial wall becomes stiffer. Because of this relation, arterial compliance should therefore not be given as a single independent variable.

It is possible to calculate arterial cross-sectional compliance based on the Bramwell and Hill equation by using pulse wave velocity as an index of arterial stiffness and measuring intra-arterial blood pressure. With this approach, taking blood pressure into account as a variable, other investigators have actually come to conclusions similar to those presented in this report, i.e., there is no difference in forearm arterial compliance between hypertensive and normotensive subjects.

As already stressed, mechanical properties of muscular arteries such as the radial artery do not necessarily reflect the behavior of proximal elastic arteries. This may be particularly true in hypertensive patients. Indeed, the large elastic arteries are the preferential site of the deleterious effects of high blood pressure, leading to an increase in cardiovascular morbidity and mortality. Therefore, further comparative compliance measurements were needed in elastic arteries. The observations made in rats, in contrast to those obtained in humans, concerned the elastic carotid arteries. Furthermore, the hypertensive animals exhibited a quite severe blood pressure elevation compared with the normotensive controls without any overlap between the groups. Notwithstanding, in these experimental animals, no difference in the diameter-pressure relation could be detected between the normotensive and hypertensive groups. At near-matching blood pressures, the arterial compliance and distensibility were actually lower in the hypertensive than in the normotensive rats. These findings are in good agreement with the results regarding arterial distensibility in stroke-prone SHR. This is certainly not yet understood. Unlike normotensive and hypertensive subjects, who are members of a continuous blood pressure distribution, WKY rats and SHR belong to different populations with distinct blood pressure distributions. It may therefore not be surprising if some small differences exist between the two strains in terms of arterial compliance and distensibility.

The results of the present investigations, with use of a novel, high-precision echo-tracking device, provide no evidence for a difference in arterial cross-sectional compliance or distensibility in the forearm between newly diagnosed hypertensive and normotensive subjects as well as between young hypertensive and normotensive rats at the carotid artery. These results suggest that mechanical alterations of these conduit vessels are not causal in the development of hypertension.

References


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