Arterial Alterations With Aging and High Blood Pressure: A Noninvasive Study of Carotid and Femoral Arteries

A. Benetos, S. Laurent, A.P. Hoeks, P.H. Boutouyrie, and M.E. Safar

Noninvasive in situ evaluations of pulsatile changes of blood pressure and arterial diameter were performed at the sites of the common carotid and femoral arteries in a population of 78 untreated normotensive and hypertensive subjects. Arterial segments were studied by using an original echo-tracking technique for internal diameter and validated applanation tonometry for local pulse pressure measurements. Whereas mean arterial pressure is known to be identical in all parts of the arterial tree, pulse pressure was significantly lower in the carotid (52.7 ± 2.2 mm Hg) than in the brachial (62.0 ± 2.0 mm Hg) or femoral (62.5 ± 2.5 mm Hg) arteries. Despite a higher pulse pressure and diastolic diameter, the femoral artery had a lower pulsatile change in diameter (3.47 ± 0.18% versus 6.07 ± 0.28%; p < 0.0001) and distensibility coefficient (9.36 ± 0.58 versus 21.60 ± 1.75 × 10^-3 kPa^-1) than the carotid artery. Local cross-sectional compliance of the carotid artery was higher than that of the femoral artery (7.42 ± 0.46 versus 6.20 ± 0.28 m^3·kPa^-1·10^-7; p < 0.05). Whereas age was strongly correlated with arterial parameters at the site of the carotid artery (pulse pressure: r = 0.54, p < 0.0001; pulsatile change in arterial diameter: r = -0.62, p < 0.0001; distensibility coefficient: r = -0.70, p < 0.0001), no significant correlation was observed at the femoral artery. Mean blood pressure was the second factor of carotid artery alterations: the higher the mean blood pressure, the lower the distensibility of this artery (r = -0.36, p < 0.01). Since no atherosclerotic lesions were detected in the studied subjects, it is suggested that, for the same mean arterial pressure 1) the common carotid artery is exposed to lower pulse pressure than the common femoral artery, 2) the common carotid artery is a highly compliant artery with a strong alteration of its viscoelastic properties with age, and 3) the common femoral artery has smaller mechanical “buffering” properties than the carotid artery, with little influence by aging. This study provides evidence that the effects of aging and elevated blood pressure differ substantially in the different portions of the arterial tree.

KEY WORDS • pulsatile changes of arterial diameter • pulsatile changes of blood pressure • echo-tracking techniques • tonometry • hypertension • aging

Alterations of large arteries are a major factor of cardiovascular morbidity and mortality.1 Aging, hypertension, and other risk factors such as diabetes, hyperlipidemia, and smoking can alter the structural and functional properties of the arterial wall. The principal changes that occur with aging are arterial dilation, increase in wall thickness, and decrease in elasticity and compliance.2 It is well known that large arteries have not only a conduit but also a “buffering” function.3 Because of their distensibility, they can dampen the pulsatile systolic output of the ventricle. Indeed, after left ventricular ejection has distended the aorta and its larger branches and the aortic valves have closed, the elastic aorta and its branches recoil, thereby sustaining the pressure head and rendering the blood flow to the periphery steadier than it otherwise would be. This buffering function is a result of the viscoelastic properties of the arterial wall. Age and hypertension are reported to alter the elastic properties and to decrease arterial compliance.2,4 However, the arterial tree is not a homogeneous system. Major differences exist in the structure and function of various arteries. Moreover, the incidence and causes of atherosclerotic lesions differ among the aortic, carotid, femoral, and coronary arteries.

Animal studies have shown major differences in the mechanical properties of various arterial segments.2,3 In humans, similar findings may be deduced from clinical and arteriographic investigations. However, human studies are limited for methodological reasons, principally because of the invasive nature of evaluation techniques.6 Recent progress in noninvasive echo Doppler ultrasound has enabled more adequate evaluation of the viscoelastic properties of large arteries by using transcutaneous measurements in situ.7-12 The geometry and the mechanical properties of specific arterial segments may be investigated in situ, but such studies have yielded poor results in patients with hypertension.

The aim of the present study was to estimate the effects of age and blood pressure level on the viscoelas-
tic properties of two different arteries: the common carotid artery and the common femoral artery. Arterial diameter and its pulsatile changes were evaluated by using an original noninvasive echo-tracking system, whereas systolic–diastolic variations in blood pressure on the same arterial segments were measured with applanation tonometry.

Methods

Patients

Seventy-eight subjects (42 men and 36 women) were included in the study. Of these subjects, 52 had mild to moderate essential hypertension and 26 had no past history of high blood pressure and were considered normotensive subjects. Mean±SEM age was 47±6 years (range, 23–71). Weight and height (mean±1 SEM) were 71±2 kg and 168±1 cm, respectively. In all hypertensive patients, treatments were discontinued at least 21 days before the study, and diastolic blood pressure (by conventional sphygmomanometry) remained above 90 mm Hg throughout this ambulatory washout period. Patients had no sign, symptom, or history of cardiac, renal, or cerebrovascular accident or major diseases other than hypertension. On the basis of conventional echocardiography, no stenosis >30% of the lumen area or atheromatous plaque of the common, internal carotid, or iliofemoral arteries was noticed. The evaluation of velocities with a continuous Doppler device confirmed the absence of any significant lesion of the studied segments. Thus, although all of the included patients had normal arteries from the clinical and ultrasonic points of view, this study could not accurately evaluate the thickness of the arterial wall, and it is possible that wall thickening was more pronounced in some of the studied segments than others. The cardiothoracic ratio on chest x-ray was within the normal range. Plasma glucose, total cholesterol, and high density lipoprotein cholesterol were constantly within the normal range. Ten subjects smoked. None of the 78 subjects used antidiabetic or hypolipidemic medication. Informed consent was obtained from each subject after a detailed description of the procedure. The protocol was approved by INSERM (Institut National de la Santé et de la Recherche Médicale). Each subject was investigated in a controlled environment of 22±1°C. After 20 minutes of rest in the supine position, systolic and diastolic blood pressures and heart rate were determined every 2 minutes by an oscillometric recorder (model 845, Dinamap, Critikon, Tampa, Fla.) positioned at the right arm. The same parameters were also measured with a mercury sphygmomanometer on the right arm. Mean arterial pressure (MAP) was estimated by the formula MAP=DBP+(SBP-DBP)/3, where DBP and SBP are diastolic and systolic blood pressure, respectively. Then arterial measurements, including noninvasive evaluation of systolic–diastolic variations of arterial diameter and blood pressure, were performed at the sites of the right common carotid and common femoral arteries. Diameter and pressure changes were studied successively but exactly at the same point. A marker was used to localize the site of the arterial segment.

Systolic–Diastolic Variations of Arterial Diameter

The vessel wall motion of the arteries was measured by using 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 enables the transcutaneous assessment of the displacement of the arterial wall during the cardiac cycle and, hence, the time-dependent changes in arterial diameter relative to its initial diameter at the start of the cardiac cycle. The availability of the electrocardiogram (ECG) trigger facilitates the detection of the peak distension of the artery relative to its initial diameter. The lowest and highest values within 300 msec after the occurrence of the ECG trigger are taken as the minimum and maximum values of the distension waveform, respectively. This procedure can detect the diastolic and systolic peak diameters in both carotid and femoral arteries. Based on the twodimensional B-mode image, an M-line perpendicular to the artery was selected. The radiofrequency signal of three 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 may have temporarily entered the selected sample volumes, thus obscuring the vessel wall signal, a tracking system was developed that allowed the vessel walls to be tracked by the sample volumes. Then the displacement of the arterial wall was 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 common carotid artery is shown in Figure 1: the successive values of the stroke change in diameter during systole (Ds–Dd), the end-diastolic diameter (Dd), and the relative stroke change...
in diameter ([Ds−Dd]/Dd) were computed from the
recording.

With this procedure, the side of measurement did not influence the values of arterial dimensional data. For instance, in 17 normotensive subjects, no significant difference was observed between measurements performed on the left and the right common carotid arteries (7.0±0.2 mm, 0.45±0.03 versus 7.0±0.2 mm, 0.44±0.02 mm, and 6.6±0.5% versus 5.4±0.4% for Dd, Ds−Dd, and [Ds−Dd]/Dd, respectively). All arterial dimensional data given in the present study were from the right artery.

The reproducibility of the method was studied in five normotensive subjects. The coefficient of variation (standard deviation expressed as a percentage of the mean of several successive measurements) was used for this purpose. First, reproducibility was assessed during the recording of three to eight successive cardiac cycles as shown in Figure 1. The mean±SEM coefficients of variation determined under these conditions were 1.0±0.3%, 6.0±0.1%, and 6.0±0.1% for Dd, Ds−Dd, and (Ds−Dd)/Dd, respectively. (Variations in absolute values were 72±18 μm for diameter and 25±1 μm for systolic-diastolic changes.) Second, reproducibility was assessed during 12 measurements performed by each of two observers over a 90-minute period in five subjects. Each measurement of the 12 was the mean of three to eight values corresponding to three to eight cardiac cycles. Under these conditions, the mean intraobserver coefficient of variation was 3.0±0.1%, and 8.0±0.1% for Dd, Ds−Dd, and (Ds−Dd)/Dd, respectively. The interobserver coefficient of variation was 5.0±0.1%, 10.0±0.1%, and 12.0±1.0% for Dd, Ds−Dd, and (Ds−Dd)/Dd, respectively. (Variations in absolute values were 362±7 μm for diameter and 42±0.5 μm for systolic-diastolic changes.)

Systolic–Diastolic Variations of Blood Pressure

To improve the accuracy of noninvasive recording of the arterial pressure wave contour, we used a pencil-type probe incorporating a high-fidelity strain-gauge transducer (Millar Instruments Inc., Houston, Tex.). The transducer has a small pressure-sensitive area (0.5x1.0 mm) with a frequency response >2 kHz that is coplanar with a larger area (7-mm diameter) of flat surface that is in contact with the skin overlying the pulse.

The instrument uses the principle of applanation tonometry as it is used in oculomotor tonometry for registration of intraocular pressure. In principle, flattening (applanation) of a curved surface that is subject to internal pressure allows direct measurement of the pressure within the structure. The wall flattening is important, since the force vectors from the intra-arterial pressure must be evenly distributed to the force-sensing area without distortion from the circumferential stresses inherent in a curved wall. With applanation achieved, the circumferential forces are rendered normal to the direction of the probe and hence balanced. An applanated artery supports on a rigid bony structure thus provides a contact force between the skin and the sensor area equal to the intra-arterial pressure. The contact force is converted to an electrical signal by the transducer, thus providing a continuous beat-to-beat recording.

FIGURE 2. Scatterplot shows invasive intra-aortic pulse pressure versus carotid artery pulse pressure recorded with applanation tonometry.

Because the tonometer transducer is small relative to the size of the artery, the positioning of the transducer over the site of the artery was found to be an important consideration in clinical investigation. First, movement of the transducer introduced by the operator’s hand or movement of the subject may cause artifacts. This can easily be prevented by the use of a stereotaxic system to fix the probe and by the operator’s being relaxed and comfortable. Second, the hold-down force should be just enough to achieve adequate applanation. Excessive force leads to two characteristic changes. It is initially accompanied by a gradual increase in the pressure levels recorded in late diastole with a distortion of the diastolic part of the wave shape, often seen as a sharp negative deflection before the succeeding systolic upstroke. The change in the value of systolic pressure recorded at this stage was usually minimal. The second characteristic change caused by a further increase in hold-down force is the inversion of the systolic peak. The third source of artifact was caused by the angulation between the probe and vessel. This particularly affects the systolic part of the pressure wave. Ideally, the
were slightly lower than those obtained with a sphygmomanometer.

**Statistical Analysis**

All values are given as mean±SEM. Comparison of arterial parameters was done with an analysis of variance (ANOVA) followed by an unpaired Student's t test. The effects of age, blood pressure, and other studied parameters on elastic arterial properties were tested with single or multiple regression analysis. The level of significance was p<0.05.

**Results**

**Mean Values of Hemodynamic Parameters**

Table 1 shows the brachial blood pressure determinations. As already reported, Dinamap measurements were slightly lower than those obtained with a sphygmomanometer. However, mean arterial pressure was not significantly different using the two methods. Pulse pressure measured by sphygmomanometer was 61.2±2 mm Hg. We showed in "Methods" that this value was strongly correlated with radial pulse pressure as measured by applanation tonometry.

Table 2 summarizes the mean values of arterial parameters. Pulse pressure was significantly higher in the femoral (62.5±2.5 mm Hg) than in the carotid (52.7±2.2 mm Hg) artery (p<0.0001). The femoral artery had a higher diastolic diameter (p<0.0001) and a lower pulsatile change in arterial diameter (p<0.0001) than the carotid artery. These differences led to a twofold lower distensibility coefficient in the femoral compared with the carotid artery (p<0.001) for the same level of mean arterial pressure.

**Relations of Carotid Artery Parameters**

Figures 3, 4, and 5 show the changes in carotid artery parameters as a function of age. With aging, carotid pulse pressure significantly increased (r=0.53; p<0.0001) (Figure 3). Pulse pressure recorded at the site of the brachial artery did not show any increase with age. Diastolic diameter of the carotid artery increased significantly with age (r=0.39; p<0.001) (Figure 4A),

**FIGURE 3. Scatterplot shows pulse pressure changes of the carotid artery with aging. ○, Normotensive subjects; ●, hypertensive subjects.**
whereas pulsatile change of diameter decreased as a function of age ($r = -0.61; p<0.0001$) (Figure 4B). These changes led to a strong linear decrease in the distensibility coefficient of the carotid artery with age ($r = -0.70; p<0.0001$) (Figure 5A). Cross-sectional compliance significantly decreased with age, but to a lesser degree than distensibility (Figure 5B). The respective roles of age and mean blood pressure levels on the carotid artery parameters were evaluated using stepwise regression analysis (Table 3). In this model, age is the more powerful factor influencing carotid artery changes. Mean blood pressure level is the second significant factor for such alterations: the higher the mean blood pressure, the higher the arterial diameter ($r = 0.37; p<0.01$) and the lower the distensibility coefficient ($r = -0.36; p<0.01$). The correlations observed between the elastic properties of the carotid artery and age were significant for both normotensive and hypertensive subjects. No statistical difference in these slopes for the two populations was observed (Figures 4 and 5).

Height and weight after adjustment for blood pressure and sex did not influence the carotid artery parameters. Women had a lower carotid artery diameter (6.39±0.15 mm versus 7.07±0.15 mm in women and men, respectively; $p<0.002$). No significant relation was observed between pulse pressure and pulsatile changes of the carotid artery diameter.

**Relations of Femoral Artery Parameters**

No changes in femoral artery pulse pressure (Figure 6) or pulsatile changes in diameter (Figure 7) were observed with age. Arterial diameter showed a slight increase with aging, but this relation was not significant ($p=0.10$). Mean blood pressure levels did not influence any of these measured parameters.

Stepwise regression analysis showed that gender is an important factor for femoral artery diameter differences (8.24±0.24 versus 9.74±0.21 mm in women and men, respectively; $p<0.001$). A positive relation was observed between pulse pressure and pulsatile changes of the femoral artery diameter ($r=0.27; p<0.05$).

**Discussion**

The present investigation was designed to evaluate the arterial parameters of the common femoral and carotid arteries in a selected group of 78 normotensive
TABLE 3. Percent Contribution of Age and Mean Blood Pressure to Carotid Artery Parameter Changes by Stepwise Regression

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age (%)</th>
<th>Mean blood pressure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>8.4*</td>
<td>7.7*</td>
</tr>
<tr>
<td>(Ds-Dd)/Dd (%)</td>
<td>32.5†</td>
<td>7.9*</td>
</tr>
<tr>
<td>Distensibility coefficient</td>
<td>50.8†</td>
<td>14.3†</td>
</tr>
<tr>
<td>Cross-sectional compliance</td>
<td>24.3†</td>
<td>1.2 (NS)</td>
</tr>
</tbody>
</table>

\[(D_s-D_d)/D_d, \text{ relative stroke change in diameter.}\]

\[^{*}p<0.002.\]

\[^{†}p<0.0001.\]

\[\text{NS, not significant.}\]

and hypertensive subjects with two specific characteristics. On the basis of clinical and biological investigations, and particularly on the basis of thorough echo Doppler determinations, all these subjects were shown to have no significant atherosclerotic complications. Indeed, the aim of the design was to study two peripheral large arteries for the same level of mean arterial pressure, a parameter that is known to be nearly the same in all parts of the arterial tree. The three major conclusions from the study are 1) that the pulsatile component of blood pressure greatly differed in the brachial, the carotid, and the femoral arteries; 2) that the geometric parameters of the carotid and femoral arteries greatly differ, with the latter having a more rigid arterial wall; and 3) that age influences the carotid but not the femoral artery. Such findings were observed by using new noninvasive methods to investigate pulsatile changes in blood pressure and arterial diameter on the same arterial segments.

Applanation tonometry has been shown to be an accurate means of measuring peripheral wave contour. The noninvasively measured carotid pulse contours and invasively measured ascending aortic pulses have been shown to have close similarities in both the time and frequency domains. Direct measurement of carotid pulse pressure by applanation tonometry reveals that the alteration in the pulsatile component of blood pressure is underestimated by the measurements of brachial artery sphygmomanometric blood pressure.

Indeed, the brachial artery pulse pressure is higher than that of the carotid artery as extensively shown by invasive studies and confirmed by the present study. The contour of the aortic pressure alters as it travels toward the peripheral arteries. Whereas the mean blood pressure is only slightly lower in peripheral than in central arteries, the pulse pressure has a greater amplitude. In the normal human, the amplification of pulse pressure between the aorta and brachial artery averages 18–31%, and that between the aortic and radial arteries, 46%. The modifications of pulse pressure between central and peripheral arteries depend principally on nonuniform arterial elasticity of arteries and on peripheral wave reflections. With advancing age in humans there is a gradual stiffening of arteries, an increase in pulse wave velocity, and an increase in pulse wave reflections. As these changes more involve the aorta and central arteries than peripheral arteries, there is little amplification of the pressure wave between central and peripheral arteries, and central and peripheral pulse pressures tend to be equal in older subjects. Using the Millar tonometer, Kelly et al showed that the amplitude of the carotid wave increased by 91.3% from the first to the eighth decade compared with only a 67.5% increase in the radial pulse. The results of the present study are in agreement with Kelly et al and show that carotid pulse pressure increased strongly with age. Interestingly, no comparable findings were observed at the sites of the brachial or the femoral arteries.

In recent years, several devices have been described to transcutaneously measure arterial diameter and wall motion by tracking the echo signals from both the anterior and posterior arterial walls. Arndt et al first reported completely noninvasive measurement of arterial diameter by means of a pulsed ultrasound technique. The echoes backscattered by the arterial walls were tracked by a gated threshold detector. Later, Hokanson et al developed a phase-locked tracking device that permitted the selection and tracking of a particular zero crossing within the vessel wall echoes. Earlier instruments used ultrasound methods that had...
several drawbacks. Superimposed echoes from the tissue surrounding the artery as well as imperfect position of the ultrasound beam perpendicular to the arterial wall caused major unpredictable changes in the amplitude of the echo waveform. Moreover, the resolution of the method was relatively poor and did not allow the recognition of some well-known relations between arterial changes and age. Newer instruments are characterized by sufficient linearity, dynamic range, and tracking speed even when the signal-to-noise ratio of the original signal is not high. The device used in the present study was substantially improved with the help of the Doppler shift to evaluate wall motion, thus permitting a high degree of reproducibility. The values of arterial parameters are quite similar to those previously reported in the literature, particularly at the sites of the carotid and femoral arteries.

In addition to the increase in pulse pressure with age observed at the site of the carotid artery, pulsatile changes of arterial diameter significantly decreased with aging, leading to profound alterations in the mechanical properties of this artery. This alteration was clearly expressed by a strong negative linear relation between the distensibility coefficient and age (Figure 5A). Thus, an increase in age of 10 years decreased distensibility by 30%. Carotid cross-sectional compliance was also altered by age but to a lesser degree than the distensibility coefficient (Figure 5B). This was due to the concomitant increase in the diastolic arterial diameter as a function of age (Figure 4A). We can, therefore, suggest that arterial dilation partially counteracts the strong alteration of elastic properties induced by aging. Similar observations have been reported in animal studies. In addition to age, blood pressure also influenced carotid artery alterations. In our study, blood pressure seemed to be less important than age. However, the importance of blood pressure levels should not be underestimated; in our population, after adjustment for age, an increase in diastolic blood pressure of 20 mm Hg led to a decrease in distensibility of 20%. This is consistent with the well-known acceleration by hypertension of age-induced changes in arterial parameters. Previously reported results show that even in borderline hypertensive subjects there is a decrease in elastic arterial properties. In our study the effects of aging were similar in normotensive and hypertensive subjects. However, larger population studies are needed to determine whether the effects of aging and blood pressure levels are similar in normotensive and hypertensive subjects.

In the present study, we observed that the femoral artery was much less elastic than the carotid artery. This finding confirms previously reported data from animal and human studies and has been attributed to differences in histopathological structures, However, with age the carotid artery becomes much stiffer and tends to reach the low distensibility levels of the femoral artery, since the latter is not clearly altered by aging (Figure 8). This result could be surprising, because the femoral artery is a common site of atherosclerotic lesions and is frequently affected by cardiovascular risk factors. At this point, two remarks should be made. First, the incidence of smoking (major risk factor for lower-limb atherosclerotic lesions) was very low in our study (13%). Second, all patients with echocardiographic signs of atheromatous plaque were excluded. However, as we suggested earlier in this article, the classic echo Doppler methods we used for the detection of atherosclerotic stenotic lesions could not eliminate other types of structural lesions, such as intimal-medial thickening. Therefore, the observed changes in arterial distensibility as a function of age could be modulated by the presence of atherosclerotic disease as well as chronic exposure to elevated blood pressure. Changes in the femoral and carotid arteries may in fact reflect a more profound alteration secondary to these factors. Such findings point to the importance of the intrinsic modifications of the arterial wall in the pathophysiology of aging and elevated blood pressure in humans.

In conclusion, the carotid artery is a very compliant artery in young patients with low blood pressure. With aging and an increase in blood pressure, a strong decrease in the elastic properties of this artery occurs. Arterial dilatation partially counteracts these alterations. On the other hand, the femoral artery is a much less compliant artery, and it is not as affected by aging and high blood pressure.

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References
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