Intrinsic Stiffness of the Carotid Arterial Wall Material in Essential Hypertensives

Caroline Bussy, Pierre Boutouyrie, Patrick Lacolley, Pascal Challande, Stéphane Laurent

Abstract—We have previously shown that the decrease in large artery distensibility observed in patients with essential hypertension (HT group) was primarily due to an increase in distending pressure and not to hypertension-associated structural modifications of the artery, suggesting a functional adaptation of the wall material. To evaluate the elastic properties of the wall material of the common carotid artery, we determined Young’s incremental elastic modulus (Einc) in the HT group and in normotensive subjects (NT group) as a function of blood pressure and circumferential wall stress. In 102 HT patients with never-treated essential hypertension and 40 age- and gender-matched NT subjects, the Einc-pressure and Einc-stress curves were calculated from intima-media thickness and from diameter and pressure waveforms, determined with echo tracking and aplanation tonometry, respectively. The “effective” stiffness of the wall material, determined through Einc calculated at mean blood pressure, was significantly higher in the HT than in the NT group. The “intrinsic” stiffness of the wall material, determined through Einc calculated at a common circumferential wall stress, did not differ between the 2 groups. However, when each group (HT and NT) was analyzed according to tertiles of age, the “intrinsic” stiffness of the arterial wall material was increased only in younger HT patients. In middle-aged and older HT patients, the intrinsic mechanical properties of the carotid arterial wall material were unchanged, and the increased stiffness of the common carotid artery in the HT group was due primarily to the increased level of blood pressure. These results also indicate that the deleterious effects of aging and hypertension on “intrinsic” stiffness are not additive. (Hypertension. 2000;35:1049-1054.)

Key Words: arteries ■ arterial stiffness ■ elastic modulus ■ hypertension, essential

The increased arterial stiffness observed in patients with essential hypertension (HT group) is generally attributed to arterial wall hypertrophy.1–3 However, our group4–8 and others9–11 have shown that the increased stiffness of large arteries, observed in hypertensive humans and animals, was due to an increase in distending pressure and not to hypertension-associated changes in structural properties, suggesting a functional adaptation of the wall material.

This hypothesis was raised in experiments involving humans4–6,9,10 and animals8,9,11 comparing distensibility of normotensive (NT) and HT groups at a given blood pressure (BP), either through their diameter-pressure curves4–9 or by calculating an index supposedly independent of BP (the arterial stiffness index β)10,11 or by lowering the BP of spontaneously hypertensive rats (SHR) with anesthesia.11 Under these conditions, isotropic distensibility (i.e., that calculated at a given BP) was not significantly lower in the HT group than in the NT group. These findings suggested that sustained essential hypertension was associated with a rearrangement of the large arterial wall material, leading to “equivalent” mechanical properties in HT and NT groups.5,8 Several studies further analyzed such an adaptive mechanism and demonstrated that the incremental elastic modulus (or Young’s elastic modulus, Einc), calculated at a given circumferential wall stress, was not significantly different between HT and NT groups. Indeed, Einc evaluates the elastic properties of the material of the arterial wall, whereas distensibility gives information on the elastic properties of the artery as a hollow structure.1,3 To provide information that is dependent on the properties of the material only and independent of the way in which the material is arranged, the elastic modulus should be calculated for a given circumferential stress. Under these conditions, no significant increase in Einc was observed in the HT group.5,8 This was shown in humans at the site of a distal muscular artery and the radial artery5 and in adult SHR at the site of the abdominal aorta8 and indicated that wall materials of both populations or strains had equivalent mechanical properties.

However, such a direct comparison has never been made at the site of a large elastic artery in humans. Proximal large elastic arteries sustain the major part of the heart-vessel coupling.1,2 In addition, proximal elastic arteries enlarge with hypertension in humans5,8,10,12 in contrast to distal arteries in humans5 and to the carotid artery7 and the aorta6,11 in adult SHR. This arterial enlargement in HT patients, which is
associated with a higher circumferential wall stress,10,12 may alter the elastic properties of the artery by spatially rearranging the various components of the arterial wall and changing the vectorial pathway of force transmission.

Thus, the objectives of the present study were to determine Einc of the common carotid artery (CCA) in never-treated HT patients and to compare Einc between HT patients and age- and gender-matched NT subjects at a given circumferential wall stress. We also studied the interactions between aging and hypertension by analyzing HT and NT groups according to tertiles of age.

**Methods**

**Patients and Subjects**

One hundred forty-two subjects were included in the present study: the NT group consisted of 40 normal subjects aged 23 to 76 years, and the HT group consisted of 102 patients aged 34 to 70 years with never-treated ambulatory hypertension. The HT population consisted of ambulatory patients referred to the Hypertension Unit of Broussais Hospital. The diagnosis of essential hypertension was established by the presence of an increase in BP (>140 mm Hg systolic BP [SBP] and >90 mm Hg diastolic BP [DBP]) and the absence of clinical or laboratory evidence suggestive of secondary forms of hypertension. Hypertension was diagnosed as sustained on the basis of several BP measurements made successively by the general practitioner referring the patient to Broussais Hospital and by the physician specialists examining the patient in the outpatient clinic and day hospital of Broussais Hospital. NT subjects were derived from medical personnel and their family with a supine SBP <140 mm Hg and DBP <90 mm Hg. All subjects were free of clinical evidence of coronary artery or cerebrovascular disease. No patients with valvular heart disease, arrhythmias, or renal disease were included. The study was approved by the institutional review committee of Broussais Hospital, and the subjects gave informed consent. The procedures followed were in accordance with institutional guidelines.

**Arterial Noninvasive Measurements**

The investigation was performed in a controlled environment kept at 22±1°C after 15 minutes of recumbence. Brachial SBP and DBP were measured with a mercury sphygmomanometer (phase I and IV Korotkoff sounds).

**CCA Pressure Waveform, Internal Diameter, and Wall Thickness**

CCA pressure waveform was determined noninvasively with applanation tonometry with use of a pencil-type probe incorporating a high-fidelity strain gauge transducer (SPT-301, Millar Instruments).13–15 We previously validated local pulse pressure (PP) measurements made successively by the general practitioner referring the patient to Broussais Hospital and by the physician specialists examining the patient in the outpatient clinic and day hospital of Broussais Hospital. NT subjects were derived from medical personnel and their family with a supine SBP <140 mm Hg and DBP <90 mm Hg. All subjects were free of clinical evidence of coronary artery or cerebrovascular disease. No patients with valvular heart disease, arrhythmias, or renal disease were included. The study was approved by the institutional review committee of Broussais Hospital, and the subjects gave informed consent. The procedures followed were in accordance with institutional guidelines.

The thickness/radius ratio (percentage) was calculated as 2h/Di, where h is mean wall thickness, and Di is mean internal diameter.

**Arterial Wall Stress, Distensibility, Compliance, and Elastic Modulus**

The thickness/radius ratio (percentage) was calculated as 2h/Di, where h is mean wall thickness, and D is mean internal diameter. Mean circumferential wall stress (σθ, in kilopascals) was calculated according to Lamé’s equation as follows: σθ = MBP × D/2h, where MBP is mean BP, calculated as MBP = DBP + ((SBP − DBP)/3). The diameter-pressure curve of the CCA was noninvasively determined within the diastolic-systolic range, as previously described with slight modifications. Diameter and pressure waveforms were recorded for 15 seconds in immediate succession at the same site. Carotid MBP, derived from the area under the curve of the carotid pressure waveform, was set equal to brachial MBP. Then, carotid SBP and DBP were calculated from carotid MBP and PP.6 Both waveforms were processed in parallel with a similar algorithm and synchronized. Then, the luminal cross-sectional area (LCSA)-pressure curve was fit by using an arctangent model, and the cross-sectional distensibility-pressure and compliance-pressure curves were calculated either at MBP (DistMBP and CompMBP, respectively) or at 110 mm Hg (Dist110 and Comp110, respectively).6

The Einc (Young’s modulus), which provides direct information about the elastic properties of the wall material that is independent of the vessel geometry,1,13 was calculated as previously described.6,8 as Einc = (3(LCSA/WCSA))/Dist, where LCSA is a function of BP, WCSA is the mean wall cross-sectional area, and Dist is the cross-sectional distensibility, expressed as a function of BP. The Einc-pressure and Einc-stress curves were determined within the diastolic-systolic range. The “effective” elastic properties of the wall material were determined through Einc calculated at the respective MBP (EincMBP) of the HT and NT groups. The “intrinsic” elastic properties of the wall material were determined through Einc, either calculated at a common distending BP, 110 mm Hg (Einc110), or at a common circumferential wall stress (Eincw).

We compared this novel method of pressure-diameter curve determination (measurement of pressure and diameter in immediate succession on the same side) with the previous method (simultaneous measurement of diameter and pressure on opposite sides). The short-term within-observer within-patient repeatability16 of Einc measurements was evaluated through the mean value and the standard deviation of the difference between 2 determinations of Einc at MBP, performed at 15-minute intervals, in 15 subjects (including NT and HT subjects). Repeatability was 2 to 5 times better with the novel method than with the previous one, with mean values of the difference being 0.03×103 kPa for the novel method and 0.07×103 kPa for the previous method and standard deviations of the difference being 0.09×103 kPa and 0.49×103 kPa, respectively.

In the above 15 subjects, we also assessed the short-term, within-observer, within-patient repeatability between 2 determinations of carotid parameters performed at 15-minute intervals, according to Bland and Altman.17

**Statistical Analysis**

Data are expressed as mean±SD, except in figures. Quantitative variables were compared by means of an unpaired Student t test, and categorical variables were compared by means of a χ² test. To compare distensibility at the same BP level in the HT and NT groups, respective values of Dist110 were compared, and a significant downward (or upward) shift of the distensibility-pressure curve of HT was sought within the PP range common to the NT and HT groups (100 to 120 mm Hg), as previously described.5,6 The same procedure was followed for the comparison of the diameter-, compliance-, and Einc-pressure curves and Einc-stress curves between the NT and HT groups. The HT group was compared with the NT group first as a whole, and then according to tertiles of age.

Multivariate regression models18 were constructed in the whole population (NT and HT subjects) and included MBP and other variables (eg, age, gender, and body surface area) and carotid PP. A robust multiple stepwise regression analysis was performed. A value of P<0.05 was considered significant. Statistical analysis was performed by using NCSS 6.0 package software (Hintze JL).

**Results**

**Repeatability of CCA PP, Diameter, Wall Thickness, and Elastic Modulus**

According to Bland and Altman,17 the mean value, the absolute difference, and the standard deviation of the difference between 2 measurements of carotid PP, performed at
TABLE 1. Clinical Characteristics of NT Subjects and HT Patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>NT Subjects (n=40)</th>
<th>HT Patients (n=102)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>47±16</td>
<td>50±10</td>
</tr>
<tr>
<td>Gender ratio, male/female</td>
<td>20/18</td>
<td>54/48</td>
</tr>
<tr>
<td>Height, m×10⁻²</td>
<td>172±9</td>
<td>167±9</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>71±13</td>
<td>72±12</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.81±0.19</td>
<td>1.82±0.23</td>
</tr>
<tr>
<td>Smoking, yes/no</td>
<td>6/32</td>
<td>14/88</td>
</tr>
<tr>
<td>Fasting glycemia, mmol/L</td>
<td>5.38±0.76</td>
<td>5.56±0.62</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>6.18±1.16</td>
<td>6.21±1.23</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>4.16±0.93</td>
<td>4.03±1.04</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.37±0.34</td>
<td>1.45±0.47</td>
</tr>
<tr>
<td>Brachial BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>115±11</td>
<td>153±22*</td>
</tr>
<tr>
<td>MBP, mm Hg</td>
<td>86±8</td>
<td>119±12*</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>71±7</td>
<td>99±10*</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>68±10</td>
<td>72±10</td>
</tr>
<tr>
<td>Carotid BP</td>
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<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>118±14</td>
<td>166±24*</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>70±7</td>
<td>95±12*</td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>48±15</td>
<td>71±24*</td>
</tr>
</tbody>
</table>

Values are mean±SD. BSA indicates body surface area.

*P<0.0001.

15-minute intervals, were 51.1, 0.6, and 5.1 mm Hg, respectively. For Einc at MBP, these values were 0.82, 0.03, and 0.09×10⁻¹ kPa. For internal diameter, stroke change in diameter, and wall thickness, the absolute difference between measurement 1 and measurement 2 did not exceed 5.4% of the mean value.

Arterial Pressure and Geometry

The 2 groups were comparable as far as age, gender ratio, height, weight, body surface area, smoking, fasting glycemia, and total, LDL, and HDL cholesterol were concerned (Table 1). Brachial SBP, DBP, and MBP and carotid SBP, DBP, and PP were significantly higher in HT than in NT subjects (Table 1). Internal diastolic diameter and LCSA at MBP were significantly higher in HT than in NT subjects, but LCSA was not different between the 2 groups at 110 mm Hg (Table 2). Carotid IMT, WCSA, and circumferential wall stress were significantly higher in HT than in NT subjects (Table 2), whereas the thickness/radius ratio was not significantly different between the groups. In multivariate analysis of HT and NT groups considered as a whole, carotid IMT was significantly related to carotid PP (P<0.001) after adjustment for age (P<0.001), but it was not related to brachial PP.

Distensibility, Compliance, and Elastic Modulus as a Function of BP

Distensibility, pressure at MBP was significantly lower in the HT group than in the NT group (Table 2). In the HT group, although the distensibility-pressure curve was shifted toward higher levels of BP, a large part of it still overlapped the NT curve (data not shown). No significant downward or upward shift was observed for the HT group, and for a given level of BP (110 mm Hg), distensibility was not significantly different between the HT and NT groups (Table 2). Similar results were observed when compliance-pressure curves, CompMBP and Comp110, were compared between the HT and NT groups (Table 2).

Einc increased as BP was elevated during the cardiac cycle (data not shown). EincMBP was significantly higher in the HT group than in the NT group (Table 2). No significant downward or upward shift of the Einc-pressure curve was observed in the HT group, and Einc110 was not significantly different between the HT and NT groups (Table 2). Einc increased as circumferential wall stress increased during the cardiac cycle (Figure 1). Einc was significantly higher in the HT group than in the NT group at their respective mean circumferential wall stress (Figure 1 and Table 2). No significant downward or upward shift of the Einc-stress curve was observed in the HT group, and for a given wall stress (65 and 80 kPa, values corresponding to the mean wall stress of the NT and HT groups, respectively), Einc was not significantly different between the groups (Table 2). In univariate analysis, EincMBP and Einc110 were positively and significantly correlated with aging in each group (for EincMBP, r=0.8 and P<0.001 for NT subjects and r=0.42 and P<0.0001 for HT patients; for Einc110, r=0.8 and P<0.001 for NT subjects and r=0.24 and P<0.01 for HT patients).

Analysis of PP and Carotid Elastic Properties According to Tertiles of Age

PP and carotid elastic properties of the HT and NT groups were compared according to tertiles of age: younger NT (aged 36±7 years), middle-aged NT (aged 46±7 years), and older NT (aged 62±7 years) subjects and younger HT (aged 39±7 years), middle-aged HT (aged 50±7 years), and older HT (aged 61±7 years) patients. The gender ratio did not differ between the HT and NT groups for any tertile of age. The brachial/carotid PP ratio, an index of the PP amplification phenomenon, decreased significantly (P<0.01) with aging: from 1.19±0.27 in younger NT to 0.90±0.28 in older NT subjects and from 0.94±0.24 in younger HT to 0.79±0.24 in older HT patients. For each tertile, the brachial/carotid PP ratio was lower in the HT group than in the NT group (P<0.01).

The distensibility-pressure curve was shifted downward for older NT subjects compared with younger NT subjects (P<0.001, data not shown). The curve of middle-aged NT subjects had an intermediate position. A similar downward shift with aging was observed in the HT group (P<0.05, data not shown).

As shown in Figure 2, the Einc-stress curve for the NT and for HT group was shifted upward with aging (P<0.001), with an overlap of the HT curve on the NT curve in the tertile of older patients. The same overlap was observed in middle-aged subjects in the HT and NT groups. However, the Einc-stress curve for the younger HT subjects was shifted upward (P<0.01) compared with the curve for the younger NT subjects, indicating an increased intrinsic stiffness of the arterial wall material in younger HT subjects only.
The present study, designed to compare the elastic properties of the carotid arterial wall material in HT and NS groups, provides the first evaluation of the Einc-stress curve of both HT and NT groups, carotid Einc was higher in younger HT than in younger NT subjects, whereas it did not differ between the HT and NT groups in middle-aged and older individuals.

**Discussion**

The present study, designed to compare the elastic properties of the carotid arterial wall material in HT and NS groups, provides the first evaluation of the Einc-stress curve of both HT and NT groups, carotid Einc was higher in younger HT than in younger NT subjects, whereas it did not differ between the HT and NT groups in middle-aged and older individuals.

**Consideration of Methods**

The method used to noninvasively establish the in vivo diameter-, distensibility-, compliance-, and Einc-pressure curves has been considered in detail previously, either in humans or in rats. To our knowledge, this is the first study in which the Einc-stress curve of the carotid artery was established in humans under physiological conditions.

The accuracy of the measurement of PP with aplanation tonometry has been previously validated and was exemplified in the present study by 2 findings. First, the brachial/carotid PP ratio, an index of the PP amplification phenomenon, decreased significantly with aging in the NT and HT groups and was significantly lower in the HT group than in the NT group at any given age. Second, in multivariate analysis of the HT and NT groups considered as a whole, carotid Einc was significantly related to carotid PP after adjustment for age but was not related to brachial PP.

A brachial/carotid PP ratio less than unity in hypertensives may appear at first surprising, according to the classical physiology and pathophysiology of wave reflections. One possibility is that in the present study, carotid PP was overestimated and/or brachial PP was underestimated compared with intra-arterial PP. In a previous study, we found an intercept of only 0.4 mm Hg between carotid PP (measured with aplanation tonometry) and aortic PP (measured during catheterization), indicating no underestimation of carotid PP. However intra-arterial forearm PP has been reported to be underestimated by oscillometric and sphygomanometric measurements by 10 to 15 mm Hg.

The accuracy of the echo-tracking method for the measurement of internal diameter and its systolic-diastolic changes has been validated previously. Our repeatability results indicate that carotid PP, mean internal diameter, and IMT measurements can be used in cross-sectional clinical studies for the calculation of Einc, either at MBP or 110 mm Hg, provided that they are performed by an experienced investigator following a standardized protocol.

In the present study, because of the feature of the radio frequency (RF) signal analysis by the Wall Track System, we measured carotid IMT and not total arterial wall thickness. Thus, we may not have taken into account, in the analysis of the mechanical properties, the possibility of extramedial atherosclerotic changes. In addition, the ultrasonic measurements of carotid IMT does not allow us to differentiate between the intimal changes related to atherosclerosis, which may increase stiffness, and the medial changes, which may tend to normalize wall stress. Carotid atherosclerosis should be taken into account, because hypertension is a risk factor. However, atherosclerosis develops to a lower extent at the site of the CCA than at the carotid

**TABLE 2. Arterial Parameters of the CCA in NT Subjects and HT Patients**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>NT Subjects (n=40)</th>
<th>HT Patients (n=102)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid parameters at MBP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal diameter, m x 10^-3</td>
<td>5.10±0.85</td>
<td>5.62±0.79</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LCSA, m^3 x 10^-6</td>
<td>25.1±7.1</td>
<td>29.1±8.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Stroke change in diameter, m x 10^-6</td>
<td>4.05±161</td>
<td>341±114</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Relative stroke change in diameter, %</td>
<td>6.7±2.8</td>
<td>5.1±1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Wall thickness, m x 10^-6</td>
<td>4.93±135</td>
<td>528±130</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WCSA, m^2 x 10^-2</td>
<td>8.0±3.4</td>
<td>11.5±3.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thickness/radius ratio, h/r</td>
<td>0.20±0.06</td>
<td>0.21±0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Circumferential wall stress, kPa</td>
<td>64.8±20.3</td>
<td>79.7±20.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CS distensibility, kPa^-1 x 10^-3</td>
<td>22.6±14.9</td>
<td>10.7±7.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CS compliance, m^2 x kPa^-1 x 10^-7</td>
<td>6.0±3.1</td>
<td>3.6±1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Einc, kPa x 10^3</td>
<td>0.71±0.29</td>
<td>1.04±0.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Carotid Parameters at 110 mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCSA, m^3 x 10^-6</td>
<td>26.9±7.3</td>
<td>28.5±8.2</td>
<td>NS</td>
</tr>
<tr>
<td>CS distensibility, kPa^-1 x 10^-3</td>
<td>13.2±7.7</td>
<td>13.4±24.5</td>
<td>NS</td>
</tr>
<tr>
<td>CS compliance, m^2 x kPa^-1 x 10^-7</td>
<td>3.4±2.4</td>
<td>4.2±5.8</td>
<td>NS</td>
</tr>
<tr>
<td>Einc, kPa x 10^3</td>
<td>1.16±0.31</td>
<td>1.02±0.29</td>
<td>NS</td>
</tr>
<tr>
<td>Einc at a given wall stress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 kPa, kPa x 10^3</td>
<td>0.73±0.30</td>
<td>0.92±0.28</td>
<td>NS</td>
</tr>
<tr>
<td>80 kPa, kPa x 10^3</td>
<td>1.04±0.32</td>
<td>1.35±0.33</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD. CS indicates cross-sectional; h/r, mean wall thickness/radius; and NS, not significant.
The arterial wall is not homogeneous and is composed of various elements, including smooth muscle cells, collagen, elastin, and various components of the extracellular matrix. All of these elements contribute to the mechanical behavior of the wall material through their own elastic modulus and the way in which they are arranged.1,3 Because the spatial arrangement of wall components is dependent on the level of circumferential wall stress1,3 and because carotid mean circumferential wall stress was higher in the HT group than in the NT group, we compared Einc between both groups at a common circumferential wall stress.

We calculated the Einc-stress curve of the CCA according to the same methodology as previously published for use in rats.8 Thus, we determined the mechanical properties of an equivalent material that occupies the same space than the real one. This material is supposed to be homogeneous, isotropic, and incompressible. We also hypothesized that the artery was cylindrical. Using these hypotheses, we were able to use a well-known method from mechanical engineering that calculates the parameters of interest for thick-wall tubes.5,8

Because we carefully selected never-treated patients with sustained essential hypertension, the increase in CCA IMT very likely reflects structural changes specific for essential hypertension.

**Interpretation of Findings**

The main finding of the present study is that at a given circumferential wall stress common to both HT and NT groups, carotid Einc was higher in young HT than in young NT individuals, whereas it did not differ between middle-aged and older HT and NT individuals.

To our knowledge, this is the first time that an increased “intrinsic” stiffness of the arterial wall material has been shown in patients with essential untreated hypertension and has been found to be restricted to younger HT patients. A BP-independent increase in arterial stiffness has already been described in secondary hypertension. Indeed, patients with end-stage renal disease and treated hypertension have a lower carotid artery distensibility than do NT individuals for a given BP.21 Wistar rats with renovascular hypertension have a higher elastic modulus than do their age-matched controls at a given wall stress.22 The mechanisms underlying such an increase in arterial stiffness in younger HT patients are unknown. The analysis of the wall material elastic properties according to tertiles of age1,12,13,23 indicates that the deleterious effects of aging and hypertension on intrinsic stiffness are not additive. Thus, the mechanisms involved in the arterial stiffening in younger HT patients likely differ from those advanced to explain the stiffening of large arteries with aging.1,12,13,23 Including fragmentation of elastin fibers, fibrosis, and accumulation of advanced glycation end products on both elastin and collagen fibers.

It is generally accepted that more severe and/or long-standing hypertension is more likely associated with an increased intrinsic arterial stiffness than is newly diagnosed never-treated hypertension in otherwise healthy individuals.12 An increased intrinsic stiffness of the aortic wall material has been reported in old (15 months) but not in adult (5 and 9 months) SHRs compared with Wistar-Kyoto rats.23 Thus, that the increased intrinsic arterial stiffness was restricted to younger HT and not to older HT properties of the wall material.1,3

**Figure 1.** Mean carotid artery elastic modulus–stress curves in 40 NT subjects (shaded circles) and 102 HT patients (open circles). Values are expressed as mean±SEM. Elastic modulus was significantly higher in HT than in NT subjects at their respective mean circumferential wall stress. No significant downward or upward shift was observed in the HT group, and for a given wall stress (65 or 80 kPa, values that correspond to the mean wall stress of NT and HT groups, respectively), the elastic modulus was not significantly different between the HT and NT groups.

**Figure 2.** Mean carotid artery elastic modulus–stress curves in NT and HT groups. Analysis according to tertiles of age is as follows: □ indicates 13 younger NT subjects; ■, 13 middle-aged NT subjects (mid NS); ▲, 13 older NT subjects; ☐, 34 younger HT patients; ◯, 34 middle-aged HT patients (mid HT); and □, 34 older HT patients. Values are expressed as mean±SEM. The NT and HT Einc-stress curves shifted upward with aging (P<0.001), with an overlap of the HT curve on the NT curve in the tertile of older patients. The same overlap was observed for mid HT and mid NS. However, the Einc-stress curve for younger HT patients shifted upward (P<0.01) compared with the curve for younger NT subjects, indicating an increased intrinsic stiffness of the arterial wall material in younger HT patients only.
subjects may appear surprising at first. However, a BP-independent increase in carotid artery stiffness has been reported in 10- to 17-year-old normotensive adolescents with a positive parental history of myocardial infarction, suggesting an influence of the genetic background on arterial elastic properties. Such a genetic influence is likely in the present study.

Our results also suggest that adaptive mechanisms are activated in middle-aged and older HT patients, in whom the intrinsic mechanical properties of the carotid artery wall material are unchanged, compared with age-matched NT individuals. In these HT patients, the increased stiffness of the CCA in hypertension is due primarily to the increased level of BP. The overlap of the HT and NT Einc-stress curves, in the middle-aged and older tertiles, indicates that wall materials in the HT and NT groups have similar mechanical properties and can be considered equivalent. These results are consistent with previous data obtained in HT patients at the site of a distal muscular artery, the radial artery, and in adult SHR at the site of the abdominal and thoracic aortas.

The mechanisms underlying the equivalence of CCA wall material in middle-aged and older HT and NT individuals are unclear. They may involve a spatial reorganization of the network of wall components (smooth muscle cells, elastin, and collagen fibers) through changes in fibronectin, which plays an important role in cell-matrix interactions through specific cellular integrin receptors. In SHR, the increase in fibronectin and αβ3 density might reflect an increased number of mechanical attachments between the extracellular matrix, cells, and collagen fibers within the media. In addition, the percentage of cell surface connected to the elastic lamellae through dense plaques was 2-fold higher in SHR than in Wistar rats, indicating a higher number of attachments to distensible components.

In conclusion, the results of the present study indicate an increased “intrinsic” stiffness of the arterial wall material in younger HT patients but not in middle-aged and older HT patients compared with age- and gender-matched NT individuals. They also indicate that the deleterious effects of aging and hypertension on intrinsic stiffness are not additive.

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References
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