Basis for the Altered Arterial Wall Mechanics in the Spontaneously Hypertensive Rat

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SUMMARY Carotid and tail arteries from 20-week-old spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY) were used to compare mechanics and biochemical properties. Measurements of pressure-diameter relations were made on isolated segments under conditions of active (145 mM K+) and passive (0 mM Ca++ and 2 mM EGTA) smooth muscle. Connective tissue, water and electrolyte contents, and extracellular water spaces were determined. Chemical data were also obtained from segments of thoracic aorta. The passive mechanics of arteries from the SHR were stiffer compared to those from WKY. Total connective tissue content (collagen + elastin) and collagen/elastin ratio were both smaller in the SHR arteries. Differences in the characteristics of the connective tissue matrix other than total content must exist in SHR and WKY arteries. Maximum values of active stress (force/area) developed by SHR arteries were larger and occurred at smaller values of wall strain compared to WKY arteries. The maximum reduction in wall diameter with smooth muscle activation was larger in the WKY arteries, but these constriction responses were better maintained at higher pressures by SHR arteries. Extracellular water space was lower in SHR arteries, while total water content was not different. The fraction of the wall of SHR arteries occupied by smooth muscle cells was larger than that of WKY arteries. When values of maximum active stress were normalized to the relative cell content, no difference was found for SHR and WKY carotids, but SHR tail arteries still produced a significantly larger active cell stress than WKY tail arteries. This suggests that intrinsic differences exist in the properties of smooth muscle cells of SHR and WKY tail arteries. (Hypertension 3: 485-495, 1981)

KEY WORDS • passive mechanics • collagen • elastin • extracellular space • connective tissue content • isolated arteries • smooth muscle mechanics • cell volume

THERE is general agreement that changes in arterial wall properties occur associated with developed hypertension.1-2 These changes involve the passive stiffness properties of the arterial wall as well as the maximum-force-generating capacity of arterial smooth muscle. However, there is some disagreement with regard to the nature of these changes, as well as to whether they are the cause or the result of hypertension.

It is generally accepted that the passive stiffness of the arterial wall is increased in established hypertension. However, recent studies by Berry and Greenwald3 and from this laboratory5-6 suggest that a decrease in stiffness may occur at least initially in arteries from genetically hypertensive as well as experimentally hypertensive animals. Berry and Greenwald3-4 further suggest that this increase in compliance of arteries from hypertensive animals is a result of a decrease in the ratio of collagen to elastin content. A previous study from this laboratory reported increased stiffness of carotid arteries from spontaneously hypertensive rats (SHR) compared to its control counterpart, the Wistar-Kyoto rat (WKY), but with no differences in connective tissue content.7

Most investigators have found that maximum values of active force developed by arteries from hypertensive animals were lower than that of control animals.8-9 Some of these studies involved descriptions of the complete active length-tension curve of these preparations10 and documented that these differences were not simply due to differences in initial muscle length but that the entire active length-tension curve was depressed in hypertensive arteries.10 Recently, however, Mulvany and Halpern11 found an increase in active force development in mesenteric arterioles from SHR. However, when normalized on the basis of wall cross-sectional area, they found no
significant difference in the values of maximum active wall stress (force/area) for control and hypertensive arteries. In previous studies from this laboratory, it was demonstrated that maximum values of active wall stress were elevated in arteries from genetic7 as well as from experimental forms of hypertension.6

In view of this diversity in findings, we have reinvestigated the differences in arterial wall mechanics in normotensive and spontaneously hypertensive rats. This investigation was centered on several areas to extend and explain differences previously reported. First, studies were conducted on vessels from two different locations, the carotid and tail arteries. Second, active responses were obtained using high extracellular potassium to obtain a means of activating the contractile system, which did not depend on cell membrane receptors and their properties. Third, a more detailed description of the chemistry of these arteries was undertaken to provide an explanation for the differences found.

**Methods**

**Animals**

We used 18 male SHR and 18 male WKY, obtained at 10 weeks of age from Charles River Breeding Laboratories, and maintained in our animal facility for an additional 10 weeks prior to use. The week before use, the animals were weighed and had blood pressures (BPs) measured on two separate occasions by the indirect tail-cuff method (Narco Biosystems).

The animals were anesthetized with pentobarbital (40 mg/kg i.p.), and sacrificed by exsanguination from the ascending aorta and inferior vena cava. The two carotid arteries, the entire thoracic aorta from the left subclavian branch to the diaphragm, and the tail artery were removed from the animals. The length of the carotid and tail arteries between two identifiable landmarks was measured in vivo before removal. The arteries were placed in a physiological salt solution (PSS) at 37°C, and trimmed of fat and loose connective tissue using a dissecting microscope. The PSS was aerated with a 95% O2-5% CO2 mixture and had the following composition in mM: 116.5 NaCl, 22.5 NaHCO3, 1.2 NaH2PO4, 2.4 Na2SO4, 4.5 KCl, 1.2 MgSO4, 2.5 CaCl2, and 5.6 dextrose. The arteries were placed in a metabolic shaker and maintained at 37°C by using a heater-circulator unit (Tecan Temp unit). The pressure used to inflate the segments was generated using an electropneumatic transducer (Conoflow, Model T25), which was driven from a compressed air supply at 15 psi. A current-controlled valve in the electropneumatic transducer was driven by an external electrical signal from a function generator (Hewlett Packard Model 3310B) to obtain the desired transmural pressure within the vessel segment. The segments were inflated throughout the experimental procedures with air. Previous studies suggested that this procedure (air inflation) did not produce tissue drying or chemical content alterations.13 The external diameter of these segments was measured continuously using a cantilever transducer pivoted from above.13

After mounting, the segments were allowed to equilibrate for a period of 60 minutes at zero transmural pressure. The bath was then drained and refilled with a modified PSS containing 145 mM K+ where K+ was substituted for Na+. After 10 minutes in this solution, the pressure-diameter response to slow continuous inflation at a rate of 0.1 mm Hg/sec was obtained and recorded on an XY plotter (Hewlett Packard Model 7436). For the carotid arteries, pressure was varied from 0 to 250 mm Hg, while for the tail arteries, pressure was varied from 0 to 400 mm Hg. Only the inflation response was recorded under activated conditions.

At the end of this response, the bath was drained, rinsed, and refilled with a calcium-free PSS containing 2 mM EGTA. After 30 minutes, pressure was continuously cycled between 0 and 250 mm Hg for the carotid, and 0 and 400 mm Hg for the tail arteries for 15 minutes. This time was required for complete reversal of activation and removal of all calcium stores in the tissues. Then, the response to one complete inflation-deflation cycle at a rate of 0.5 mm Hg/sec was obtained and recorded on the XY plotter. The Ca++-free data were obtained at a faster inflation rate to shorten the time required, since previous studies showed no significant rate dependence of this response when the smooth muscle was inactive.1,13 Addition of potassium or norepinephrine to the bath at this point did not produce any change in the pressure-diameter curve, suggesting the absence of smooth muscle activation under these conditions (i.e., passive). When data acquisition was completed, the vessel was removed from the bath, its unstressed length (L0) measured, and its wet weight determined using an analytical balance. Vessel lengths were measured using a dissecting microscope (Bausch and Lomb, Stereo-Zoom 7) fitted with a micrometer disc in one eyepiece.
Data Analysis

At the end of the experiment, the records from the XY plotter were used for data analysis. These pressure-diameter curves under active and passive conditions were converted to digital form using a Talos digitizer. Only data from the ascending limb of the pressure-diameter curves were used in data analysis. Digital data were transferred to a computer (PDP 11/34) for analysis. By using pressure-diameter data along with values of stressed and unstressed length and segment weight, a computer program calculated various mechanical parameters for each condition and each blood vessel. Values of wall stress (σw) were computed from transmural pressure (P) using the following equation:

$$\sigma_w = \frac{a}{b-a} P,$$

where a and b are the internal and external radii respectively. Values of b were obtained directly from values of external diameter. Values of a were obtained using values of b, stressed length, and segment wet weight. This method of analysis assumes that the deformation of these segments is isovolumetric and yields values of wall stress averaged over the entire wall thickness of the segment.

We obtained values of incremental elastic modulus (Einc) from the pressure-diameter data, assuming the arterial wall to be isotropic using the following equation:

$$E_{inc} = \frac{2a^b}{b^2 - a^2} \frac{\Delta P}{\Delta b}.$$  

where ΔP/Δb represents the slope of the pressure-radius curve at a specific point (i.e., pressure or strain). We determined the above slope at a point on the curve using a polynomial regression method based upon a least squares fit of data points above and below the one of interest, with a digital computer (PDP 11/34). We applied this analysis separately to the data recorded under active (K+) and passive (EGTA) conditions.

The effects of activation of vascular smooth muscle were quantitated in two ways. In the first, we computed the values of the active stress response as the increase in tangential wall stress at a given diameter, using pressure-diameter data for active and passive conditions and Equation 1. We performed this analysis at a variety of values of diameter and produced data that are equivalent to isometric force per unit wall area.

In the second, we computed the values of active diameter response using differences in the values of the midwall diameter at a specific value of transmural pressure for active and passive conditions. These diameter differences were normalized by dividing them by the value of the passive diameter at each pressure level. These responses have been shown to be equivalent to isobaric constriction responses for arterial smooth muscle. The validity and applicability of these methods for the study of arterial smooth muscle mechanics have been described in previous publications.

Values of the various mechanical parameters were averaged for all experiments on the two vessels from the two animal groups at specific pressure levels from 0 to 250 or 400 mm Hg in steps of 5 mm Hg. Some of the data points were eliminated from the plotted curves for purposes of clarity. All data values given herein were expressed in terms of mean ± 1 se. We used the double-ended Student t test for all statistical comparisons, taking a p value of less than 0.05 as an indication of a significant difference.

Chemical Analyses

The vessel segments used for mechanical studies were subsequently used for the determination of connective tissue content. We determined their collagen and elastin contents using Fischer and Llaurado's modified version of the method of Neuman and Logan. The segments were weighed before and after drying at 90°C for 20 hours. Collagen and elastin fractions of the arteries were separated by heat and pressure. The hydroxyproline fraction of the soluble and insoluble fractions was then determined, and used to compute the collagen and elastin contents respectively. Previous studies have demonstrated that the use of such segments for mechanical studies does not influence their subsequent analysis for connective tissue content.

The remaining segments were used to determine their water and electrolyte content, including the extracellular water space using 65Co chelated to EDTA as an extracellular marker. The arterial segments were incubated in normal PSS at 37°C for 2 hours. They were then transferred to identical solutions containing the isotopic marker for a period of 20 minutes. They were then removed, lightly blotted to remove surface water, and placed in polyethylene vials. Wet weight was determined prior to drying at 90°C for 20 hours. Dry weight was then determined. From the radioactivity taken up by the samples, the 65Co-EDTA space was assumed to be representative of the extracellular water space in the tissue. The difference between the Co-space and total water was assumed to represent the cellular water component of the tissue. The cell solid content of these arteries was estimated as the difference between total solid content and total connective tissue content. Total cell volume was then estimated as the sum of cell solid and cell water contents.

The samples used for the determination of water spaces were subsequently used for the analysis of electrolyte content. The samples were ashed in 30% peroxide at 90°C for 20 hours. The ash was then dissolved in 0.1 N HNO3 containing 0.01 M LiNO3. Electrolyte content of these samples was then determined by atomic absorption spectrophotometry using appropriate standards (Perkin-Elmer Model 303). Electrolyte content was expressed on the basis of the tissue dry weight.
Results

No significant difference existed in the body weights of the WKY and SHR groups at 20 weeks of age (table 1), although the SHRs were somewhat lighter. However, the heart weight, both in absolute terms and as a fraction of the body weight, was substantially larger in the SHR group. This is to be expected, based upon the cardiac (hypertrophy) response to increased afterload in these animals. The week before the experiments, the systolic blood pressure and heart rate were obtained while the rats were unanesthetized but restrained; results showed a significantly elevated systolic pressure in the SHR group (table 1).

Examples of on-line pressure-diameter curves obtained under active and passive conditions for carotid and tail arteries from SHR and WKY animals are shown in figure 1. Significant differences exist in the mechanical characteristics of carotid and tail arteries from the two groups. The passive pressure-diameter curve for the carotid artery was biphasic, showing an S-shaped variation. On the other hand, passive pressure-diameter curves for the tail arteries were monotonic. The active pressure-diameter curves of the carotid also showed an S-shaped behavior shifted to the left relative to the passive curve. In the case of the tail arteries under activated conditions, the initial portion of the pressure-diameter curve showed an extremely steep slope with near complete closure of the lumen. They demonstrated a very prominent plateau region where the diameter changed rapidly over a relatively small pressure range. It is of interest that the pressure range over which this plateau occurred was significantly higher in the SHR than in the WKY. A similar suggestion of a plateau also existed in the case of carotid arteries, although certainly not as pronounced as that of the tail artery.

A summary of the variation of measured external diameter with transmural pressure under passive conditions for the two arterial sites is given in figure 2. Values of external diameter for the carotid artery of the SHR were significantly smaller compared to the WKY carotids for pressures between 60 and 160 mm Hg, i.e., over the physiological range. Also, values of the external diameter for the SHR carotids were significantly larger at low values of pressure between 0 and 30 mm Hg. The total change of diameter for SHR carotids over the pressure range of 0 to 200 mm Hg was significantly smaller than that of the WKY under passive conditions. No significant differences existed in the relationship between external diameter and pressure in the case of the tail arteries for the two animal groups.

Selected passive mechanical data for arteries from the two groups are summarized in table 2, which compares the axial retraction ratios (L/L₀) for the vessels studied. In the case of the carotid artery, a much smaller axial retraction ratio was found for the SHR. While a similar situation existed for the tail arteries, the differences were not statistically significant. Data at an arbitrary reference pressure of 100 mm Hg are also summarized; values of the internal radius at 100 mm Hg pressure were significantly smaller in the case

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**Table 1. Terminal Hemodynamic Data for the Rat Groups**

<table>
<thead>
<tr>
<th>Rat group</th>
<th>Body weight (g)</th>
<th>Heart weight (g)</th>
<th>Heart wt (mg/g)</th>
<th>Systolic pressure (mm Hg)</th>
<th>Heart rate (min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WKY (n = 18)</td>
<td>285 ± 6</td>
<td>0.68 ± 0.02</td>
<td>2.31 ± 0.14</td>
<td>127 ± 4</td>
<td>393 ± 14</td>
</tr>
<tr>
<td>SHR (n = 18)</td>
<td>283 ± 6</td>
<td>0.96 ± 0.01*</td>
<td>3.40 ± 0.08*</td>
<td>181 ± 4*</td>
<td>413 ± 26</td>
</tr>
</tbody>
</table>

*Statistically significant difference between values for WKY and SHR groups (p < 0.05).
of carotids from the SHR. No difference existed in the case of the tail arteries from the two groups. The radius/wall thickness ratio was significantly smaller in the case of the SHR carotids but were not significantly different in the case of the SHR tail arteries. Therefore, the smaller internal radius of the SHR carotid arteries was the result of both a smaller external diameter and a thicker wall. Values of normalized external diameter (1 + strain) for the two arteries at 100 mm Hg are also shown in table 2. The wall strain was much smaller in the case of carotids from the SHR, suggesting a much stiffer wall. Surprisingly, however, the value of the incremental elastic modulus at 100 mm Hg was substantially smaller in the SHR compared to the WKY carotids. None of these differences was significant in the case of the tail arteries.

Table 2 also contains values of these mechanical parameters at the average value of systolic pressure given in table 1 for the two groups. The most striking

**Table 2. Passive Mechanical Data**

<table>
<thead>
<tr>
<th>Values</th>
<th>Carotid artery</th>
<th>Tail artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WKY (n = 18)</td>
<td>SHR (n = 18)</td>
</tr>
<tr>
<td>L/L₀</td>
<td>1.70 ± 0.02</td>
<td>1.59 ± 0.02</td>
</tr>
<tr>
<td>Pressure = 100 mm Hg:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a (mm)</td>
<td>0.58 ± 0.01</td>
<td>0.60 ± 0.02*</td>
</tr>
<tr>
<td>D/D₀</td>
<td>1.95 ± 0.04</td>
<td>1.72 ± 0.02*</td>
</tr>
<tr>
<td>R/h</td>
<td>9.70 ± 0.30</td>
<td>6.80 ± 0.50*</td>
</tr>
<tr>
<td>Eᵰ (10⁶ dyn/cm²)</td>
<td>10.50 ± 1.50</td>
<td>4.9 ± 0.40*</td>
</tr>
<tr>
<td>Systolic blood pressure:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a (mm)</td>
<td>0.60 ± 0.02</td>
<td>0.60 ± 0.02</td>
</tr>
<tr>
<td>D/D₀</td>
<td>2.00 ± 0.04</td>
<td>1.72 ± 0.03*</td>
</tr>
<tr>
<td>R/h</td>
<td>10.50 ± 0.40</td>
<td>9.3 ± 0.60</td>
</tr>
<tr>
<td>Eᵰ (10⁶ dyn/cm²)</td>
<td>28.0 ± 3.70</td>
<td>45.5 ± 6.20*</td>
</tr>
</tbody>
</table>

*Statistically significant differences between values for SHR and WKY (p < 0.05).

**Abbreviations:** L/L₀ = axial stretch ratio; L = in vivo segment length; L₀ = unstressed segment length; a = internal radius; D/D₀ = external diameter ratio; D₀ = passive external diameter at zero pressure; R/h = radius/wall thickness ratio; Eᵰ = passive elastic modulus; n = number of rats.

**Figure 2. Summary of transmural pressure-external diameter relations under passive conditions, for carotid and tail arteries. Mean values ± 1 se (horizontal bars) are given.**
differences were found with values of the passive elastic modulus. The latter were significantly elevated for SHR arteries because of their higher values of systolic pressure in this group.

The passive stress-normalized external diameter data obtained from carotid and tail arteries from the two animal groups are shown in figure 3. Passive curves for both arteries from the SHR were shifted to the left relative to those from the WKY group. This shift indicates a stiffer wall in the case of arteries from the SHR. The shift in this curve was substantially greater with the carotid arteries than the tail arteries from the SHR. However, in both cases, the differences between the two groups were statistically significant at all normalized diameter levels.

A summary of values of passive incremental modulus as a function of transmural pressure for the two arterial sites is given in figure 4. Values of incremental elastic modulus were significantly smaller for carotids from the SHR for pressures at and above 80 mm Hg. For the tail artery, however, no significant differences existed in the values of the incremental modulus at any pressure.

Measurement of the connective tissue content of the carotid and tail arteries, given in table 3, shows a significantly smaller collagen content of both the carotid and tail arteries from SHR. There was no significant difference in values of elastin content for these vessels. The total connective tissue content (collagen plus elastin) was significantly lower in arteries from the SHR, as was the ratio of collagen-to-elastin content. A similar situation was also found for thoracic aortas from the two groups.

Average values of pressure-diameter relations under conditions of activated and passive smooth muscle are summarized in figure 5. The differences in the effects of activation on the pressure-diameter curve for the two animal groups are much more apparent in the case of the carotids than the tail arteries. The effects of activation on SHR carotids extended the pressure-diameter curve to significantly smaller values of diameters at high pressures.

Activation of vascular smooth muscle consistently produced a reduction in values of incremental elastic modulus at specific values of transmural pressure, especially those above 80 mm Hg, as shown in figure 6. The effect of activation was more prominent in the SHR vessels, especially at higher pressure levels.

Values of active stress response are summarized in figure 7. Normalization of vessel diameter was established by setting to zero the value of the midwall diameter at which the active stress response was zero, i.e., the value of the diameter at zero pressure under activated conditions. The value of midwall diameter at which the active stress response was maximum was set to a value of one. Other values of midwall diameter were normalized accordingly. The results given in figure 7 illustrate that the entire curve relating active wall stress to wall diameter was shifted to higher values of stress for the SHR arteries compared to WKY arteries. The value of external diameter at which the maximum response occurred was substantially lower for SHR carotid arteries. Values of normalized diameter (D/D₀) for the carotid arteries averaged 1.61 ± 0.03 for the SHR, compared to 1.89 ± 0.02 for the WKY. Values for the tail arteries averaged 1.71 ± 0.04 for the SHR, compared to 1.81 ± 0.08 for the WKY, a difference that was not statistically significant.

Analysis of the active diameter response to potassium activation (fig. 8) showed significantly higher maximum values for WKY arteries. Over the low-
pressure range, the active diameter response values were consistently higher for WKY arteries, but at higher transmural pressures were consistently lower than for the SHR.

The total water and electrolyte content of the various arteries (table 4) showed no significant differences between control and hypertensive animals. Values of extracellular water based upon 65Co-EDTA distribution space were lower in the SHR arteries (table 5); the difference was significant in the case of the carotid arteries and the aorta. Derived values of cell water content were significantly larger in the case

![Figure 4](image-url)

**Figure 4.** Variation of passive incremental elastic modulus with transmural pressure. Mean values ± 1 se are given.

![Figure 5](image-url)

**Figure 5.** Effects of smooth muscle activation upon pressure-external diameter relations of carotid and tail arteries from the two animal groups. Open circles are passive data while closed squares are active data.
of the carotid arteries and thoracic aorta from the SHR. There was a greater cell solid content at all arterial sites in the SHR. The volume fraction of the wall composed of cells was greater in the case of arteries from the SHR. Values of active stress were computed on the basis of the relative cell volume of the arteries (table 6).

When the values of active wall stress were normalized for relative cell content it was found that no significant difference existed in maximum active cell stress for the carotid arteries. On the other hand, tail arteries from the SHR still developed a significantly larger maximum active cell stress even when corrected for relative cell volume.

**TABLE 3.** Connective Tissue Content of Carotid and Tail Arteries

<table>
<thead>
<tr>
<th>Vessel</th>
<th>n</th>
<th>C  (% dry wt)</th>
<th>E  (% dry wt)</th>
<th>C + E (% dry wt)</th>
<th>C/E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic aorta</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>18</td>
<td>24.6 ± 0.9</td>
<td>38.9 ± 2.4</td>
<td>62.5 ± 2.6</td>
<td>0.68 ± 0.03</td>
</tr>
<tr>
<td>SHR</td>
<td>18</td>
<td>19.9 ± 2.0*</td>
<td>33.5 ± 3.0</td>
<td>53.5 ± 1.7*</td>
<td>0.60 ± 0.03*</td>
</tr>
<tr>
<td>Carotid artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>18</td>
<td>40.7 ± 2.5</td>
<td>31.0 ± 1.1</td>
<td>71.6 ± 3.2</td>
<td>1.36 ± 0.10</td>
</tr>
<tr>
<td>SHR</td>
<td>18</td>
<td>31.1 ± 1.6*</td>
<td>34.5 ± 2.4</td>
<td>65.0 ± 1.5*</td>
<td>0.94 ± 0.10*</td>
</tr>
<tr>
<td>Tail artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>18</td>
<td>49.8 ± 3.6</td>
<td>13.8 ± 1.3</td>
<td>63.7 ± 4.4</td>
<td>3.85 ± 0.43</td>
</tr>
<tr>
<td>SHR</td>
<td>18</td>
<td>35.5 ± 2.7*</td>
<td>15.9 ± 1.3</td>
<td>51.4 ± 2.5*</td>
<td>2.38 ± 0.35*</td>
</tr>
</tbody>
</table>

*Statistically significant difference between SHR and WKY (p < 0.05).
C = collagen; E = elastin.

**TABLE 4.** Electrolyte Content of Various Arteries (mmoles/kg dry wt)

<table>
<thead>
<tr>
<th>Vessel</th>
<th>N</th>
<th>Ca++</th>
<th>Mg++</th>
<th>K+</th>
<th>Na+</th>
<th>Cl–</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic aorta</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>18</td>
<td>20.7 ± 2.8</td>
<td>13.8 ± 1.5</td>
<td>116 ± 6</td>
<td>259 ± 21</td>
<td>369 ± 4</td>
</tr>
<tr>
<td>SHR</td>
<td>18</td>
<td>23.9 ± 2.1</td>
<td>15.5 ± 1.8</td>
<td>113 ± 7</td>
<td>265 ± 15</td>
<td>397 ± 24</td>
</tr>
<tr>
<td>Carotid artery</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>18</td>
<td>18.5 ± 3.7</td>
<td>14.4 ± 2.6</td>
<td>119 ± 7</td>
<td>317 ± 31</td>
<td>453 ± 53</td>
</tr>
<tr>
<td>SHR</td>
<td>18</td>
<td>19.7 ± 2.7</td>
<td>10.7 ± 2.7</td>
<td>116 ± 16</td>
<td>308 ± 42</td>
<td>386 ± 40</td>
</tr>
<tr>
<td>Tail artery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>18</td>
<td>25.5 ± 7.8</td>
<td>21.9 ± 2.6</td>
<td>213 ± 17</td>
<td>408 ± 41</td>
<td>468 ± 43</td>
</tr>
<tr>
<td>SHR</td>
<td>18</td>
<td>21.8 ± 4.8</td>
<td>21.3 ± 3.0</td>
<td>211 ± 6</td>
<td>360 ± 31</td>
<td>312 ± 25</td>
</tr>
</tbody>
</table>
Discussion

These experiments document a number of differences in the properties of arteries from WKY and SHR. Under passive conditions, the carotid and tail arteries from the SHR were stiffer than those from the WKY based upon the passive stress-strain curve (fig. 3). This result is consistent with previous studies from this as well as another laboratory. Chemical analysis of connective tissue content also demonstrated the presence of significant differences between the two animal groups. There was a smaller amount of collagen in arteries from the SHR. Total connective tissue content (collagen + elastin) and the collagen/elastin ratio were both lower in arteries from the SHR.

These latter findings are not consonant with classical concepts concerning the contribution of connective tissue elements to passive arterial wall mechanics. Previous studies would predict that SHR arteries should be more compliant rather than stiffer based upon their connective tissue content. This suggests that other factors in addition to the absolute amount of connective tissue elements present in the arterial wall are important in determining passive mechanical properties. One could hypothesize a number of possible mechanisms responsible for these differences. For example, differences in the amino acid sequence of individual alpha chains of collagen, or differences in cross-linking of alpha chains, could exist. It is possible that the SHR arteries possess different genetic types of collagen, as well as differences in the organization of the collagen and elastin matrices of the arterial wall. Differences in any one of these factors could contribute to the differences in the mechanical properties of the collagen and elastin elements of these blood vessels, thereby influencing their passive mechanics.

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Water Content (g/kg wet wt)</th>
<th>Cell solids (g/kg wet wt)</th>
<th>Cell fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>60Co-space</td>
<td>Cell</td>
</tr>
<tr>
<td>Thoracic aorta</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>12</td>
<td>70.1 ± 0.6</td>
<td>42.8 ± 0.8</td>
</tr>
<tr>
<td>SHR</td>
<td>12</td>
<td>70.2 ± 0.7</td>
<td>39.0 ± 0.5*</td>
</tr>
<tr>
<td>Carotid artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>10</td>
<td>71.1 ± 1.3</td>
<td>49.6 ± 0.8</td>
</tr>
<tr>
<td>SHR</td>
<td>12</td>
<td>70.3 ± 1.4</td>
<td>44.5 ± 0.6*</td>
</tr>
<tr>
<td>Tail artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>14</td>
<td>76.9 ± 1.7</td>
<td>54.2 ± 2.3</td>
</tr>
<tr>
<td>SHR</td>
<td>16</td>
<td>75.4 ± 1.0</td>
<td>50.5 ± 1.5</td>
</tr>
</tbody>
</table>

*Statistically significant differences in values between SHR and WKY groups (p < 0.05).
Some differences also exist in the results of these experiments and those previously reported.7 Previously, no significant differences were found in the connective tissue content of carotid arteries from 15-week-old male WKY and SHR. Also, the passive stiffness of the SHR carotids was greater than that of WKY carotids. In the present study, collagen content, collagen-elastin ratio, and total connective tissue content were all lower in SHR compared to WKY arteries from 20-week-old animals. This more recent finding is in agreement with results of Greenwald and Berry.4 The reasons for the differences in this study compared to the previous one7 are not clear but could be due to age differences in the animals or to changes in the genetic composition of the population. This is only speculative at best.

The results of these experiments confirm those previously reported from this laboratory concerning differences in norepinephrine-induced active stress development by carotid arteries from WKY and SHR.7 In this current study, maximum values of active wall stress development were significantly higher for both carotid and tail arteries from the SHR compared to the WKY in response to high K+ activation. As indicated above, a portion of this greater active wall stress can be ascribed to a relatively larger cell fraction in SHR arteries. When active force development was normalized on the basis of relative cell content, no difference in the maximum values of active cell stress development was found in the case of the carotid arteries. However, maximum values of active stress development for the tail arteries normalized on the basis of cell volume were still higher in the SHR.

There are a number of possible explanations for the difference in active cell force development, including geometrical as well as biochemical factors. The most likely explanation relates to the actomyosin content of the individual cells in these vessels. An increase in the concentration of actomyosin in individual cells could explain the greater active cell stress development found for the tail artery of the SHR. Recently, however, Seidel11 demonstrated that no significant differences existed in the values of aortic actomyosin content per cell in normotensive and spontaneously hypertensive rats. The possibility that differences in actomyosin content exist at different arterial sites in the WKY and SHR has not been determined to date.

Another potential explanation relates to the means used to activate the smooth muscle in this study. High extracellular potassium can be expected to produce depolarization of vascular smooth muscle cells and activation of the contractile system as a result of the influx of extracellular calcium.22 It is also possible that high extracellular potassium could depolarize nerve terminals in the adventitia of these blood vessels, thereby releasing norepinephrine stores. Part of that neuronally released norepinephrine could add a component of activation to the direct effect of the K+ on

### Table 6. Maximum Values of Active Stress on Cellular Volume Basis

<table>
<thead>
<tr>
<th>Artery</th>
<th>Active wall stress (10^3 dyn/cm²)</th>
<th>Cell fraction (%)</th>
<th>Active cell stress (10^3 dyn/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>785 ± 58</td>
<td>29.8 ± 1.5</td>
<td>2.6 ± 0.2</td>
</tr>
<tr>
<td>SHR</td>
<td>1016 ± 86*</td>
<td>36.2 ± 1.8*</td>
<td>2.8 ± 0.2</td>
</tr>
<tr>
<td>Tail</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WKY</td>
<td>1143 ± 253</td>
<td>30.8 ± 2.7</td>
<td>3.5 ± 0.8</td>
</tr>
<tr>
<td>SHR</td>
<td>1776 ± 223*</td>
<td>37.6 ± 1.7*</td>
<td>4.7 ± 0.6*</td>
</tr>
</tbody>
</table>

*Statistically significant differences in values for WKY and SHR (p < 0.05).
the muscle. If the tail arteries from the SHR had a
greater norepinephrine content or if the cells were
more responsive to the release of such norepinephrine
stores, one might find an explanation for these results.
Recent studies by Mulvany and Halpern have
indicated greater active force development of small
mesenteric arteries from the SHR. When normalized
for the larger cross-sectional area in the SHR, however,
these authors found no difference in active
wall stress development. More recently, these authors
reported that no difference in relative cell content ex-
isted for mesenteric arteries from the SHR and
WKY. Therefore, when active force development
was normalized on the basis of cell cross-sectional
area in this preparation, they concluded that no
differences exist in active cell stress for the two groups.
This conclusion is the same as the one obtained herein
for the carotid artery from SHR and WKY. The
reason for the difference in the tail artery remains to
be explained.

The results of the present experiments are similar to
those previously reported from this laboratory. In
the previous study, activation was produced by norepi-
 nephrine. Carotid arteries from the SHR produced
approximately a 28% greater maximum active stress
compared to WKY carotids. This number is similar to
the difference in maximum active stress observed in WKY arteries in response to high potassium ac-
tivation (+29%). This would be consistent with the in-
terpretation of a larger maximum active stress
development in the SHR being due to a larger relative
cell content and not to differences in cellular mem-
brane properties per se, although these experiments
certainly cannot rule out that possibility as well.

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