Aortic Compliance in Human Hypertension

Zhaorong Liu, Chih-Tai Ting, Shuxiong Zhu, and Frank C.P. Yin

Aortic compliance in normotensive and hypertensive Chinese subjects undergoing diagnostic cardiac catheterization was compared by using a newly described method that allows for determination of the pressure dependence of compliance if one assumes a value for the exponential coefficient of the pressure-volume relation of the large arteries. Under baseline conditions in the normotensive and hypertensive groups at mean aortic pressures of 96.3 and 128.6 mm Hg, aortic compliance averaged 1.47 and 0.80 ml/mm Hg, respectively. Compliance in the hypertensive group at a diastolic pressure of 99.4 mm Hg (which was nearly equal to the mean normotensive pressure) was 1.072 ml/mm Hg—still significantly lower than in the normotensive group. During nitroprusside infusion, however, the compliances in the hypertensive group increased to levels equal to or greater than those in the normotensive group. Thus, these data confirm that aortic compliance is lower in hypertensive than in normotensive humans. They further demonstrate that the lower compliance cannot be attributed entirely to the elevated blood pressure, suggesting that excess smooth muscle tone may be partly responsible. (Hypertension 1989;14:129–136)

Compliance is an important property of the arterial system. It is one measure of the properties of the walls of the vasculature, is a component of the load faced by the ventricle, and is a determinant of the configurations of the pressure and flow waves. Abnormalities in compliance can greatly affect cardiovascular function. For example, decreased compliance results in an increase in systolic and a decrease in diastolic aortic pressure—both of which are deleterious to the heart. The increased systolic pressure is an extra load during cardiac ejection and the decreased diastolic pressure can diminish coronary flow under certain conditions.

There has been great interest in quantifying total arterial compliance.1-13 The accuracy of the values of compliance quoted in these studies is, however, questionable and has not been validated because it is extremely difficult to accurately measure the total arterial blood volume. In addition, compliance is a nonlinear function of pressure.2-4 For these reasons, most of the data on arterial compliance are estimates based on simple models of the arterial system, usually a two- or three-element Windkessel. Compliance most commonly has been estimated by first assuming it is independent of pressure, and by further assuming that diastolic aortic pressure decays exponentially with a time constant equal to the product of resistance and compliance.1-3,6,7,10-12,14-20 This method is useful because resistance can be relatively easily measured. Several studies using this method have shown that compliance is decreased in hypertensive patients.15,16,18-20 We recently demonstrated, however, that this method of estimating compliance has severe limitations, primarily because the compliance estimates are critically dependent on the pressure decay being an exact monoeponential function of time.13 In reality, however, this decay is often not a true monoeponential function. For example, the presence of early diastolic reflected waves or noise in the pressure tracing causes considerable deviation from exponentiality. This not only renders these estimates inaccurate but also results in considerable variation. Hence, compliances estimated with this method could be erroneous.

Compliance has also been estimated from central aortic pressure and flow tracings by parameter estimation techniques based on simple lumped parameter models of the circulation.6,21-23 This method avoids the drawbacks of assuming an exponential pressure decay but again assumes no pressure dependence of compliance and suffers from the
uncertainty associated with all such regression methods regarding uniqueness of the resulting estimates.

We recently proposed an alternative method for estimation of arterial compliance\textsuperscript{13} that was also based on a Windkessel model of the system but was shown to have two major advantages over existing methods. First, because it used the systolic and diastolic areas under the pressure-time curve rather than the shape of the curve, it rendered the estimates less susceptible to noise and other artifacts. Second, with certain reasonable assumptions, the pressure dependence of compliance could be expressed explicitly. To obtain the pressure dependence of compliance by this method, however, required an explicit mathematical expression for the relation between arterial pressure and volume that could not be obtained experimentally in vivo. Specifically, for an exponential type pressure-volume relation of the form \( V = m e^{bp} + n \), compliance is shown to depend on \( b \) but not on \( m \) or \( n \). If we assume that values of \( b \) for all large arteries are similar and have a limited range, once \( b \) was determined from pressure-volume studies in isolated segments of large arteries, we could use those values to estimate the in situ arterial compliance.

In the present study, we first determined in dog arteries how the exponential coefficient \( b \) is affected by vasodilation and vasoconstriction (see Appendix). Using these values and those previously obtained in normal human arteries as a guide, we then estimated the ranges of arterial compliance under resting conditions in normal subjects and in hypertensive subjects during acute vasodilation with nitroprusside and after acute \( \beta \)-adrenergic blockade with propranolol.

**Subjects and Methods**

The study population comprised normotensive and hypertensive Chinese subjects undergoing diagnostic cardiac catheterization. The aortic impedance data for these subjects were described earlier.\textsuperscript{24} The study was approved by a clinical research review committee and informed consent was obtained from each subject. Criteria for categorization into normotensive and hypertensive groups as well as details on the methodology for catheterization, data acquisition, and the experimental protocols can be found in this earlier publication. Briefly, after routine diagnostic catheterization, a catheter with a micromanometer and electromagnetic flowmeter was placed into the ascending aorta. Pressures and flows were recorded on FM tape for off-line analysis. Recordings were made in both groups of patients in the resting state, and in the hypertensive group after intravenous nitroprusside and after acute \( \beta \)-blockade with propranolol (0.15 mg/kg).

The flows and pressure were digitized at 250 Hz and analyzed with software previously developed in our laboratory. The nonlinear pressure-dependent values of arterial compliances for each condition were estimated with the method we proposed in an earlier study.\textsuperscript{13} The pertinent expressions are presented here for completeness. The governing equation for a two-element Windkessel during diastole (for clarity the downstream pressure term is omitted) when there is no inflow into the system is

\[
C \frac{dP}{dt} + P/R = 0
\]

where \( C \) is compliance, \( P \) is the aortic pressure, and \( R \) is peripheral resistance. If \( C \) is pressure dependent, then integrating Equation 1 over the diastolic period, \( t^* \leq t < T \), where \( t^* \) is end systole and \( T \) is end-diastolic yields

\[
\int_{t^*}^{T} \left[ C \frac{dP}{dt} + \frac{P}{R} \right] dt = 0
\]

The integral of \( P \) over the diastolic period is simply the area under the diastolic portion of the pressure curve, \( A_d \). Thus, Equation 2 becomes

\[
\int_{P^*}^{P_s} C dp + A_d/R = 0
\]

where \( P^* \) and \( P_s \) denote the arterial pressure at the end of systole and diastole, respectively. As was shown in Reference 13, the peripheral resistance can be expressed in terms of the systolic and diastolic areas under the pressure curve as \( R = (A_s + A_d)/SV \). Hence, the right hand side of Equation 3 can be rewritten as \( SV \cdot A_d / (A_s + A_d) \).

Since \( C = dV/dP \), the integrand in Equation 3 becomes \( dV \) and the result of the integration is

\[
V(P_d) - V(P^*) = SV/K
\]

If the arterial volume is an exponential function of pressure of the form

\[
V = m e^{bp} + n
\]

then the expression for compliance is

\[
C = bm e^{bp}
\]

Using Equation 5, we can write

\[
V(P^*) - V(P_d) = m[e^{bp_d} - e^{bp_s}]
\]

Using Equation 4, we see that

\[
m = (SV/K) \{ e^{bp_s} - e^{bp_d} \}
\]
A particularly useful number is the extrapolated compliance at zero pressure, which consists of all the terms in Equation 9 except the exponential in the numerator, which equals one when P=0. Although this is not an achievable pressure, it is useful for comparison purposes since the compliance at any other value of pressure is simply this extrapolated value times \(e^{bp}\).

Note that although three coefficients are needed to completely define this nonlinear arterial pressure-volume relation, and \(mb\) is needed to define compliance, only \(b\) is needed for the in vivo estimation of the nonlinear dependence of compliance on pressure. However, since it is not possible to directly measure the overall arterial volume, to estimate compliance one must obtain values for \(b\) from studies in other large arteries and assume that these values are applicable to in situ.

We have previously shown that the coefficient \(b\) is nearly invariant for many large arteries. However, it is not clear that these values of \(b\) obtained in normal subjects are applicable in hypertensive patients since there appears to be some level of increased vasomotor tone associated with hypertension. Thus, we first studied isolated segments of dog arteries to see how \(b\) was affected by both vasodilation and vasoconstriction. The details of this methodology and results are summarized in the Appendix. Having shown that the values of \(b\) under baseline conditions were similar to those previously reported for humans and having delineated a range of \(b\) produced by vasoactive drugs, we then felt reasonably comfortable that \(b\) for hypertensive humans was within this range.

To compare the relative sensitivity of compliance with both \(b\) and pressure in the physiological range, we first calculated for each subject the compliance at four different pressures: the extrapolated zero pressure and the mean, peak systolic, and end-diastolic pressures. At each pressure, we calculated the compliances using \(b=-0.01\), which is the average of the values in human aortas and large arteries under baseline conditions. Assuming that the hypertensive group had more vasoconstriction than the normal group, we also estimated baseline compliances and those after \(\beta\)-blockade with \(b=-0.005\), which was the value found in dog femoral arteries during vasoconstriction with norepinephrine (see Appendix). Finally, we also estimated the compliances in the hypertensive group after vasodilation using \(b=-0.015\), which was the average value found in the dog femoral artery during vasodilation with nitroprusside (see Appendix). Thus, although we do not know the precise value of \(b\) in hypertensive aortas, we have probably covered a reasonable possible range that it might have.

Since each subject served as his own control, statistical comparisons of the effects of drugs within each group were performed using paired \(t\) tests. Comparisons across the groups were made using unpaired \(t\) tests and analysis of variance with repeated measures where appropriate. When significant group differences were found, pairwise comparisons were made using both the Tukey and Neuman-Keuls post hoc methods. Differences were considered statistically significant at the \(p=0.05-0.10\) range.

Results

Baseline data for the seven normotensive and 11 hypertensive subjects are summarized in Table 1. Listed are the stroke volume and the mean, peak systolic, and end-diastolic pressures along with their corresponding compliances, assuming that \(b=-0.01\). In addition, the extrapolated compliances at zero pressure \(C_0\) are also listed. The results for each subject in the hypertensive group for \(b=-0.01\) are listed along with the group average for \(b=-0.005\). Except for the compliance at extrapolated zero pressure \(C_0\), the compliances of the hypertensive group at the other pressures are significantly lower than in the normal group. Moreover, the compliances at nearly equal pressures (i.e., \(C_0\) for the normotensive group vs. \(C_m\) for the hypertensive group with \(b=-0.01\)) in the hypertensive group were still lower than in the normotensive group. These data suggest that the alterations in compliance in the hypertensive group were not solely due to the higher level of blood pressure.

The hemodynamic results in the hypertensive group during nitroprusside infusion are summarized in Table 2. The compliances calculated with \(b=-0.01\) for both baseline and drug infusion along with those with \(b=-0.005\) for baseline and \(b=-0.015\) for nitroprusside are listed. In the former case, the compliances at all three pressure levels in the hypertensive group were significantly increased during nitroprusside infusion. In the latter case the compliances were significantly increased at all pressures except peak systole. Regardless of which value of \(b\) was used, the compliances in the hypertensive group at a comparable pressure (i.e., \(C_0\) in the hypertensive group vs. \(C_m\) in the normotensive group) were now equal to or slightly greater than those in the normotensive group. Thus, nitroprusside not only eliminated the baseline differences but also increased the hypertensive compliance to levels higher than that at the same pressure in the normotensive group. These data suggest that smooth muscle tone plays a significant role in the compliance alterations in hypertension.

We have previously shown that acute \(\beta\)-blockade with propranolol produced an increase in resistance and wave reflections in the hypertensive group. These findings suggest that this drug would, if anything, increase vasoconstriction. Table 3 summarizes the effects of \(\beta\)-blockade on arterial com-
pliability for values of $b$ of $-0.01$ and $-0.005$. In both cases, $\beta$-blockade resulted in a decrease in compliance but the change was significant only at the diastolic pressure with $b=-0.01$. With $b=-0.005$, the change was significant at both extrapolated zero pressure and at the diastolic pressure.

Discussion

The extent of the arterial bed that is represented by calculations based on dynamic measurements of pressure and flow at its input is difficult to assess. Thus, it is unclear to which portion of the arterial system our compliance estimates pertain. We suspect, however, that we are estimating the compliance only of the larger arteries since clamping the aorta below the bifurcation has been shown to have minimal effect on calculated input impedance.

Our method of estimation of compliance requires a value for the exponential coefficient $b$ of the in situ arterial pressure–volume relation. This number cannot be obtained experimentally nor easily estimated in the intact circulation. Thus, presuming that our compliance estimate pertains to the larger arteries, we assumed values for $b$ based on measurements in large, normal, excised arteries. Although we do not know what effect hypertension has on this coefficient in humans, we doubt that our conclusions would be different had these data been available. First, in our previous study we showed that for many human arteries of widely varying size the range of $b$ was only from $-0.02$ to $-0.01$. Furthermore, the results in dog arteries (see Appendix) demonstrated a similar small range from $-0.01$ to $-0.005$ despite administration of potent vasoactive drugs. Thus, in normal large arteries $b$ appears to have a very limited range of values. It is unlikely that hypertension will result in a much wider range since abnormal hemodynamic parameters in these hypertensive patients could be brought within normal ranges with small doses of vasodilators. This small range for $b$ implies that the pressure–volume relations of large arteries retain their basic exponential shape since the $b$ coefficient relates primarily to the shape of the exponential pressure–volume rela-

<table>
<thead>
<tr>
<th>TABLE 1. Aortic Compliance in Normotensive and Hypertensive Subjects at Rest</th>
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<tr>
<td>Sex</td>
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<td>-------</td>
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<tr>
<td>Normotensives ($b=-0.01$)</td>
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<td>M</td>
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<td>M</td>
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<td>M</td>
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<tr>
<td>Mean</td>
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<tr>
<td>SD</td>
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<tr>
<td>Hypertensives ($b=-0.005$)</td>
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<td>M</td>
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<td>Mean</td>
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<td>SD</td>
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</tbody>
</table>

$P_m$, $P_s$, $P_d$, mean, systolic, and diastolic aortic pressures, respectively (mm Hg); $C_o$, $C_m$, $C_n$, compliances at $P_m$, $P_s$, and $P_d$, respectively (ml/mm Hg); $C_o$, compliance at extrapolate zero pressure (ml/mm Hg).

*p=0.08 vs. $C_o$ for normotensives.
tion. Whether the same holds for smaller arteries and arterioles is, of course, not known. If it is shown that compliance estimated in this manner pertains to smaller arteries, the appropriate values of \( b \) will need to be obtained by further studies.

The present study demonstrates that under baseline conditions arterial compliance is significantly lower in hypertensive compared with normotensive subjects across the entire range of pulse pressures. This was true whether we assumed values for \( b \) of \(-0.01\) or \(-0.005\) in the hypertensive group. Although we did not calculate the compliances in the hypertensive group using \( b = -0.015 \) (which was the smallest value seen during vasodilation in the dog arteries), this would have produced an even lower value of compliance, thereby further increasing the separation between the two groups.

Our conclusions are in accordance with previous results demonstrating a decreased arterial compliance in hypertensive subjects.\(^{14-18}\) Simon et al.\(^{16,17}\) using the exponential pressure decay method, found compliance values of 1.26 and 0.88 ml/mm Hg m\(^2\) in normotensive and hypertensive subjects. Messerli et al.\(^{14}\) using the simpler ratio of pulse pressure to stroke volume to index the reciprocal of compliance, found values of 0.52 in normotensive and 0.60 in borderline hypertensive subjects increasing to 0.70 and 1.6 mm Hg/ml in well-established and elderly hypertensive subjects, respectively.

We emphasize that without direct experimental validations from measurements in the intact circulation, all methods for calculation of compliance (including ours) only provide estimates. Thus, interpretations of the magnitudes of the compliance must be made carefully. Nevertheless, although it is difficult to quantitatively compare previous results with ours, the similarity of the directional alterations lends confidence that hypertension does result in this particular alteration in vascular properties. Additionally, our results suggest that the lower compliance in the hypertensive group cannot be attributed solely to the higher absolute level of blood pressure since compliance in the hypertensive group was still lower than in the normotensive group even at nearly equal pressures (Table 1). This agrees with a previous finding that the decrease in forearm compliance in hypertensive compared with normotensive humans could not be explained solely on the basis of the elevated pressure.\(^{20}\) The findings in that study are difficult to interpret unequivocally because the use of a monoexponential function to estimate compliance implicitly assumed that compliance pertained to smaller arteries and arterioles.

### Table 2. Aortic Compliance in 11 Hypertensive Subjects During Nitroprusside

<table>
<thead>
<tr>
<th>b</th>
<th>SV</th>
<th>( P_m )</th>
<th>( P_s )</th>
<th>( P_d )</th>
<th>( C_m )</th>
<th>( C_s )</th>
<th>( C_d )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>(-0.01)</td>
<td>58.5</td>
<td>128.6*</td>
<td>165.9*</td>
<td>99.4*</td>
<td>2.88†</td>
<td>0.80†</td>
</tr>
<tr>
<td>Baseline</td>
<td>(-0.005)</td>
<td>19.1</td>
<td>15.3</td>
<td>21.4</td>
<td>13.3</td>
<td>1.12</td>
<td>0.22</td>
</tr>
<tr>
<td>NP</td>
<td>(-0.01)</td>
<td>54.1</td>
<td>109.5</td>
<td>134.0</td>
<td>90.2</td>
<td>4.27§</td>
<td>1.43§</td>
</tr>
<tr>
<td>NP</td>
<td>(-0.005)</td>
<td>23.1</td>
<td>12.8</td>
<td>16.1</td>
<td>11.0</td>
<td>2.29</td>
<td>0.78</td>
</tr>
</tbody>
</table>

*Values are mean±SD. SV, stroke volume (ml); \( P_m \), \( P_s \), \( P_d \), mean, systolic, and diastolic aortic pressures, respectively (mm Hg); \( C_m \), \( C_s \), \( C_d \), compliances at \( P_m \), \( P_s \), and \( P_d \), respectively (ml/mm Hg); \( C_o \), compliance at extrapolated zero pressure (ml/mm Hg); NP, nitroprusside.

\(*p<0.002, \#p<0.02 \text{ vs. NP with } b=-0.01.\)

\(\#p=\text{NS; } Hp=0.05 \text{ VS. normotensives with } b=-0.01.\)

### Table 3. Aortic Compliance in 10 Hypertensive Subjects Before and After \(\beta\)-Blockade with Propranolol

<table>
<thead>
<tr>
<th>b</th>
<th>SV</th>
<th>( P_m )</th>
<th>( P_s )</th>
<th>( P_d )</th>
<th>( C_m )</th>
<th>( C_s )</th>
<th>( C_d )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>(-0.01)</td>
<td>60.9</td>
<td>122.8</td>
<td>157.5</td>
<td>97.0</td>
<td>3.42</td>
<td>0.98</td>
</tr>
<tr>
<td>Baseline</td>
<td>(-0.005)</td>
<td>23.9</td>
<td>15.7</td>
<td>23.4</td>
<td>13.2</td>
<td>1.50</td>
<td>0.41</td>
</tr>
<tr>
<td>IND</td>
<td>(-0.01)</td>
<td>59.7</td>
<td>126.6</td>
<td>166.0</td>
<td>99.6</td>
<td>3.20</td>
<td>0.90</td>
</tr>
<tr>
<td>IND</td>
<td>(-0.005)</td>
<td>22.0</td>
<td>15.9</td>
<td>25.6</td>
<td>12.8</td>
<td>1.42</td>
<td>0.41</td>
</tr>
</tbody>
</table>

*Values are mean±SD. SV, stroke volume (ml); \( P_m \), \( P_s \), \( P_d \), mean, systolic, and diastolic aortic pressures, respectively (mm Hg); \( C_m \), \( C_s \), \( C_d \), compliances at \( P_m \), \( P_s \), and \( P_d \), respectively (ml/mm Hg); \( C_o \), compliance at extrapolated zero pressure (ml/mm Hg); IND, inderal.

\(*p<0.02 \text{ vs. base with } b=-0.01.\)

\(\#p<0.001 \text{ vs. base with } b=-0.01.\)

\(\#p=0.04 \text{ vs. base with } b=-0.005.\)

\[\text{Liu et al} \quad \text{Compliance in Hypertension} \quad 133\]
compliance was independent of pressure. Our method does not suffer from this limitation because it can explicitly account for the pressure dependence of compliance. The advantage of being able to do so in a relatively easy manner is exemplified in the present study.

The specific cause of this abnormally low compliance in hypertensive individuals is, of course, not known and cannot be directly ascertained from the present study. Nevertheless, the results suggest that the low compliance could be attributable, in large part, to excess smooth muscle tone since the compliance at equivalent pressures was increased to normal or even supernormal values after vasodilation with nitroprusside. The fact that abnormal compliance has been found in borderline hypertensive individuals before significant elevations in pressure was interpreted to mean that there must be an intrinsic alteration in vessel wall properties. Our results are consistent with this interpretation.

Our results also demonstrate that the compliance is more sensitive to the absolute level of pressure than to the value of \( b \), at least over the pressure ranges we encountered. For example, in the hypertensive patients (Table 1) a doubling of \( b \) from \(-0.01\) to \(-0.005\) produced a maximum change in compliance values of about 40% whereas a similar change in compliance could be achieved with only a 30% change in blood pressure. Moreover, when the blood pressure fall induced during nitroprusside administration in the hypertensive group was less than 30%, there was an increase of 50% or more (e.g., \( C_u \) increased from 0.8 to 1.43, Tables 1 and 2).

It is interesting that the compliances were not as dramatically affected by \( \beta \)-blockade as were the wave reflection properties found in our previous study. Since wave reflections are a manifestation of many factors such as size, tapering, and bifurcations, in addition to altered wall properties, it appears that \( \beta \)-blockade must have more of an effect on these other variables than on compliance.

Finally, it appeared that compliance was lower in women than in men, although because the numbers were small, analysis of variance did not confirm a consistent statistically significant difference at all pressure levels and at both \( b \) values. Hence, for purposes of comparing with the normotensive group, we did not subdivide the hypertensive group by sex. Since the normotensive group consisted primarily of men, the difference between the normotensive and hypertensive groups could have been somewhat exaggerated. Clearly, further studies paying particular attention to compliance and its dependence on sex are indicated.

**Appendix**

The purpose of this section is to describe the methodology used to obtain the exponential coefficient \( b \) in the pressure–volume relation \( V = m e^{nb} + n \) for the in situ carotid and femoral arteries of dogs under baseline conditions and in the femoral artery during administration of a vasodilator and a vasoconstrictor. These data, along with similar data obtained previously in human arterial segments, will provide a guide as to a reasonable value of \( b \) to use for estimation of the overall compliance of the arterial system.

**Surgical Preparation**

Eight mongrel dogs were studied. They were anesthetized with sodium pentobarbital (35 mg/kg i.v.) and underwent a median sternotomy after being intubated and connected to a positive pressure respirator. The carotid and femoral arteries were dissected free of surrounding tissue. To enable the vessel segment to be perfused with its normal blood supply and to wash out the drugs in between runs, the proximal end of the vessel was clamped. A cannula on the leg of a y-shaped connector was then introduced into the vessel and tied in place. One arm of the y-shaped connector was introduced into the vessel upstream of the site of insertion of the cannula, and the second arm was connected to a stopcock and cannula for infusion of volume. The distal end of the vessel was prepared in a similar manner but with the arms of the y pointing downstream. One arm was reinserted into the distal site of the vessel and the other arm was connected to a cannula and pressure transducer. By clamping off the two arms of the y-shaped connectors, the vessel could be perfused with blood pumped by the heart in between runs. During each run, the upstream and downstream portions of the vessel at the sites of insertion of the cannulas were clamped to isolate the segment, and to enable flushing and infusion from a reservoir of physiological solution consisting of Krebs-Henseleit solution buffered to pH of 7.4 by bubbling with 95% \( O_2 \) and 5% \( CO_2 \).

When the vessel was isolated for study, it was first flushed free of blood and enough fluid was infused into the vessel to verify by visual inspection that there were no leaks. The vessel was then completely emptied and enough fluid was added to just distend the vessel with an intraluminal pressure of about 10 mm Hg. Fluid was then withdrawn until the pressure fell to a stable level as close to 0 mm Hg as we could reliably ascertain. The difference between these two volumes was considered the initial "unstressed" volume of the vessel. We obtained an incremental pressure–volume relation by hand injection of known increments of volume from the reservoir using an appropriately sized syringe while the pressure increment (measured with a Statham P23 ID transducer) corresponding to the volume increment was recorded on a strip chart recorder. Each increment was large enough (0.03–2.0 ml) to produce an easily measured pressure increment. After waiting 5–10 seconds for the rapid phase of stress relaxation to decay, another increment of fluid was rapidly introduced. Successive increments were added to increase the intraluminal pressure to over 200 mm Hg. We selected this
high pressure to ensure that we had sufficient data points in the nonlinear portion of the pressure-volume relation. The procedure was then reversed with decrements of volume to obtain the data during the deflation phase of the cycle. Before recording any data, four or five complete inflation-deflation cycles were performed until subsequent cycles produced reproducible results. After this "preconditioning" period, three or four complete inflation-deflation cycles were then performed. The data from these last cycles are those reported herein.

Vasoactive drugs were administered only to the femoral artery. The selected drug was added to the fluid in the reservoir. The vessel was filled with the solution, the two ends were clamped, and the pressure was allowed to equilibrate. When the pressure change due to the drug had stabilized, the vessel was emptied and the pressure-volume data were obtained as before. After completion of one drug run, the clamps were opened and blood was allowed to perfuse the segment. Enough time was allowed to ensure that the arterial pressure had reached stable, baseline levels. This typically took 15–20 minutes. The second drug was then administered via a separate reservoir and the procedure repeated. The dosage of nitroprusside used was 20 mg% and that of norepinephrine was 2.5 mg%. These doses were chosen because they produced distinct changes in the pressure-volume curves of the vessel and not necessarily because they are in the range that is commonly employed.

Data Analysis

After each volume increment, the pressure rose to a peak and then fell—rapidly at first and then more slowly to a more or less steady value due to stress relaxation. The amount of stress relaxation differed depending on the absolute pressure level and the experimental conditions but by 10 seconds a "quasi-static" level had been reached. Because of the stress relaxation, the pressure-volume data could not be obtained merely by summing each volume and pressure increment. Rather, we obtained "equivalent" pressure-volume data as follows: the difference between the peak pressure at the end of the infusion and the previously decayed value was deemed the pressure increment associated with that particular volume increment. The sum of each of

<table>
<thead>
<tr>
<th>Table A-1. Coefficients of Pressure–Volume Equation ( V = m e^{nx} + n ) for Femoral Artery of Eight Dogs</th>
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<tbody>
<tr>
<td>Femoral Artery</td>
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<td></td>
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<tr>
<td>Baseline</td>
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<td>Mean</td>
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<td>Baseline</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>SD</td>
</tr>
</tbody>
</table>

Values are mean±SD.

| p<0.05 inflation vs. deflation. |
| p<0.05 vs. nitroprusside. |
| p<0.01 vs. norepinephrine. |
| p<0.01 vs. both baseline and nitroprusside. |
| p<0.05 vs. baseline. |
| p<0.01 vs. baseline. |
these successive pressure increments together with the
sum of each volume increment (plus the
unstressed volume) yielded a series of equivalent
pressure and volume points. The coefficients of the
pressure-volume relation were obtained from these
pressure-volume data by using a modified Newton-
Raphson nonlinear estimation algorithm.

A paired t test was used for statistical comparison
of the inflation–deflation cycles for each vessel. The
effects of the two drugs compared with control in
the dog femoral artery were analyzed by using
repeated-measures analysis of variance along with
the Bonferroni correction for paired comparisons
when appropriate.

Results

Representative pressure–volume data and the
resultant fits for the femoral artery of a dog during
baseline and during nitroprusside and norepineph-
rine perfusion are shown in Figure A-1. The results
for all the dogs are summarized in Table A-1. All
three coefficients displayed hysteresis between the
loading and unloading phases of the cycle in the
baseline state and during vasoconstriction but hys-
teresis was absent for m and n during vasodilation.
Compared with both the control and nitroprusside
states, norepinephrine significantly affected the value
of b for both inflation and deflation. When the
control and nitroprusside states were compared, b
differed only during deflation.

The data for the dog carotid arteries under base-
line conditions are summarized in the lower portion
of Table A-1. The values of b do not differ between
these two arterial segments.

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