A simple theoretical approach is presented for estimating vascular distensibility of small blood vessels from noninvasively obtained pressure-flow data in the hand and forearm of human subjects. To the extent that Poiseuille's law applies to blood flow in these vascular beds, conductance (the reciprocal of vascular resistance) can be calculated from these data as the ratio of blood flow to mean arterial pressure. The fourth root of the conductance is proportional to the radius of the vascular bed. The slope of the relation between the logarithm of the radius of the vascular bed and the transmural pressure is proportional to the vascular extensibility (E), which, in turn, for small deformations and constant vascular length, is proportional to the distensibility of small blood vessel. Data obtained from the hands of six hypertensive subjects were compared with that obtained from six normotensive subjects, all with their vascular beds in a maximally dilated state. Also compared were data obtained from four normal subjects with their vascular beds in the resting state and when the beds were maximally dilated. The results indicate that 1) in the hypertensive subjects, the small blood vessels of the maximally dilated vascular bed of the hand are significantly (p<0.02) less distensible (E = 0.126 ± 0.034/mm Hg) than those in the normotensive subjects (E = 0.272 ± 0.047/mm Hg) and 2) the small blood vessels of the normal forearm at resting levels of vasomotor tone are more distensible (E = 1.00±0.38/mm Hg) than in the maximally dilated state (E = 0.51 ± 0.08/mm Hg). (Circulation Research 1988;63:572-576)
used to illustrate the theory. In both cases, the vascular bed was studied for all practical purposes, in a maximally dilated state, after an 8–10-minute occlusion of the arterial blood supply just before each flow measurement. In this state of maximal vasodilation, the vascular bed remains essentially free of sympathetic nervous control. In addition, the forearm blood flow was also studied at various values of transmural pressure (TMP) at the resting level of vasomotor tone. This was done to evaluate the level of vasomotor tone in each subject while he or she rested in a supine position in a comfortable environment. Blood flow was measured with a mercury-in-silastic strain gauge plethysmograph for the forearm and a water-filled plethysmograph for the hand. The temperature of the limb was kept constant at 31–33°C for the forearm and at 41–43°C for the hand. Blood pressure (BP) was measured at heart level in the contralateral arm with a sphygmomanometer. The mean arterial pressure (MAP) was calculated as

\[ \text{MAP} = \text{diastolic BP} + \frac{1}{3} \text{ pulse pressure} \]

TMP was calculated as

\[ \text{TMP} = P - P_s \]

where \(P\) is the pressure in the lumen of the blood vessel, and \(P_s\) is the pressure on the outer wall of the blood vessel. TMP was varied by either changing \(P\) by raising or lowering the forearm above or below the heart level or changing \(P_s\) by imposing a pressure in the chamber surrounding the hand.

From these data, it was possible to calculate a value for conductance (\(G\)) as the ratio of blood flow to mean arterial pressure

\[ G = \frac{\text{Blood flow (ml/min/100 ml tissue)}}{\text{MAP (mm Hg)}} \]

where it is assumed that the venous pressure is near zero and therefore does not contribute significantly to the driving pressure (MAP – venous pressure). However, in those instances when \(P_s\) was used to vary TMP and when \(P_s\) exceeded venous pressure, the driving pressure for blood flow was determined by the differences between MAP and \(P_s\) rather than MAP alone. It should be noted that the driving pressure in a closed system is not influenced by the effects of gravity resulting from raising or lowering the limb.

Theoretical

To the extent that Poiseuille’s law applies to the blood flow in small vessels, \(G\) is given by the formula

\[ G = \frac{\pi R^4}{8 \eta L} \]

where \(R\) and \(L\) are the internal radius and length of the blood vessel, respectively, and \(\eta\) is the blood viscosity. Then

\[ G^{1/4} = KR \]

where

\[ K = \left(\frac{\pi}{8 \eta L}\right)^{1/4} \]

which may be assumed to remain constant during an experiment. Thus, a change in \(G^{1/4}\) can be used as an index of the change in the radius of the blood vessel segment at a given value of TMP. For example, the values of \(G^{1/4}\) for a constricted vessel can be compared with that of a maximally dilated vessel at the same TMP. Such a comparison would provide information about the extent of vasoconstriction of the blood vessel. Thus, the percent reduction in radius indicating the amount of vasomotor tone may be given by

\[ \frac{G_c^{1/4} - G_r^{1/4}}{G_c^{1/4}} \times 100 \]

where \(G_c^{1/4}\) and \(G_r^{1/4}\) are the values of \(G^{1/4}\) for the vessel in the relaxed and constricted states, respectively.

In addition, when the values of \(G^{1/4}\) are obtained at various values of TMP, it is possible to obtain another important parameter, extensibility (\(E\)), which is an index of distensibility. \(E\) is defined as

\[ E = \frac{\Delta R}{R} \times 100 \]

where \(\Delta R/R\) is the unit change in radius and \(\Delta(TMP)\) is the corresponding change in the transmural pressure. It can be shown that if the vessel length remains constant under inflation and if the changes in radius are small, then \(E\) is equal to one half the distensibility (\(D\)) defined as

\[ D = \frac{\Delta V/V}{\Delta(TMP)} \times 100 \]

where \(V\) is the initial lumen volume, and \(\Delta V\) is the change in volume. It is important to point out that the value \(E\) obtained here is that of a “model” small blood vessel, which is equal to the average extensibility of all resistance vessels in a particular vascular bed.

To calculate the value of \(E\) from \(G^{1/4}\) obtained at various values of TMP, we need to start with Equation 2 and take its logarithm

\[ \ln G^{1/4} = \ln KR \]

The derivative of \(\ln G^{1/4}\) with respect to \(R\) will give

\[ \frac{d}{dR} (\ln G^{1/4}) = \frac{d}{dR} (\ln KR) = \frac{1}{R} \]

where \(K\) is a constant. Thus

\[ d (\ln G^{1/4}) = \frac{dR}{R} \]

Therefore, if we plot \(\ln G^{1/4}\) versus TMP and multiply the value of its slope by 100, we obtain the
For example, for $G^\frac{1}{4} = 0.80$ units, TMP = 75 mm Hg. For normotensive vessels and 114 mm Hg for the hypertensive vessels, both in the maximally dilated state. This means that the vessels of hypertensive subjects are stiffer than those of normotensive subjects in the vicinity of this strain level.

Figure 2 is a semilogarithmic plot of $G^\frac{1}{4}$ versus TMP for the forearm data for maximally dilated and partially constricted (because of resting vasomotor tone) vascular beds from four normal subjects. All subjects were women (average age, 34 years; average blood pressure, 114/72 mm Hg). The linear least-squares regression lines for these data are given in the figure with their equations. Recalling that $G^\frac{1}{4}$ is proportional to the radius of the vessel, it can be seen that the dilated vessels are considerably larger than their constricted counterparts. In fact, we can quantify the amount of constriction at a given TMP in the model blood vessel with Equation 4. For example, at TMP = 85 mm Hg, $G^\frac{1}{4} = 0.38$ and $G^\frac{1}{4} = 0.70$ units; thus, the amount of reduction in radius is

$$\frac{G^\frac{1}{4} - G^\frac{1}{4}}{G^\frac{1}{4}} \times 100 = \frac{R_0 - R}{R} \times 100 = 46\%$$

where $R_0$ and $R$ are the values of the radius in the relaxed and the constricted states, respectively. Again, the equations of the least-squares regression lines in Figure 2 are given in terms of the common logarithm of $G^\frac{1}{4}$. The corresponding equations in terms of the natural logarithm of $G^\frac{1}{4}$ can be obtained by multiplying each term of the equation by 2.3. When expressed in this form, the slopes of the regression lines equal one hundredth of E. Specifically, $E = 1.00 \pm 0.38/mm$ Hg for the constricted vessels and 0.51 ± 0.18/mm Hg for vessels in the maximally dilated state. Although the differences between these two values of E did not achieve statistical significance (0.10 < p < 0.20), it does suggest that the constricted vessel is approximately twice as distensible as the dilated vessel.

**Discussion**

As stated previously, our main purpose was to develop a theory to calculate distensibility of resis-
tance vessels in a maximally dilated state when they are relatively free of vasomotor tone. This goal was accomplished with Equation 10 and Figure 1.

It is important to point out that the value of E as determined from Equation 10 comes from an instantaneous value of the slope of the plot of ln G inversus TMP and does not necessarily require a linear fit to the curve (although we fit our data in Figures 1 and 2 with a linear regression line). This represents an improvement over the previous method, which requires a linear fit to the resistance versus TMP curves, at least over the range of TMP used to calculate E. Finally, we recognize that E and D, as calculated here, are not real material constants; rather, they are derived indexes that reflect compliance or stiffness of the vessel wall and have proved useful in physiology. Therefore, they provide relatively similar but not equal information as the incremental elasticity modulus $E_{inc}$, which is so often used for this purpose. We prefer to use the simple extensibility index E rather than $E_{inc}$ because many of the assumptions involved in the use of $E_{inc}$ (e.g., thin wall, linearity, and incremental isotropy) are not satisfied by an arteriole. A critical description of various elastic moduli that characterize the wall properties of a blood vessel is provided elsewhere.

The information in Figure 2, although not directly related to the main purpose of the study, represents an interesting observation. Recall the finding that the normal blood vessel was more distensible in the contracted state than when maximally dilated. Because the slope of the semilogarithmic plot shown in Figure 2 provides a value of E that reflects the status of the vascular wall at that moment, it can be used to estimate the distensibility of either maximally dilated or partially constricted vessels, as shown in the figure. In the case of constricted vessels, the value obtained for distensibility is a composite of several factors that can influence this parameter (e.g., passive elastic, neurohumoral, myogenic, etc.) and must be interpreted in this context. Although the contracted smooth muscle itself may be stiffer than its relaxed counterpart, the overall distensibility of the wall may increase as shown in Figure 2 and Mulvaney. This will happen when the level of strain in the contracted vessel is less than that in the relaxed state, possibly because of "slackening" of very stiff fibers such as collagen. Because of this reduced circumferential strain, the contracted vessel falls on the lower, more compliant portion of the stress-strain curve. In other words, the data support our argument that contracted normal blood vessels are more distensible than the fully relaxed ones at comparable levels of TMP, at least in the range of pressures shown in Figure 2.

Similar observations have been reported by Dobrin and Rovick from their study of the effect of the level of smooth muscle activity on the stiffness of muscular arteries. They compared the elastic moduli of the arterial wall after administration of norepinephrine to produce vasoconstriction and after abolishing muscle tone by administering potassium cyanide. Their study showed that at equal strain levels, the elastic modulus after norepinephrine administration was higher at all but the largest strains. On the other hand, the elastic modulus was consistently lower for the norepinephrine-activated muscle at corresponding transmural pressures. This means that the level of strain in the norepinephrine-treated vessel was much less than that in the potassium cyanide–treated vessel at the same transmural pressures, which effectively places the norepinephrine-treated vessel on the lower portion of the stress-strain curve. One would expect a directionally similar relation between the maximally dilated and contracted vascular beds as shown in our normal subjects.

It is interesting to note from Figures 1 and 2 that constricted small vessels in normal subjects have a higher vascular resistance and a greater distensibility than their dilated counterparts at the same TMP. On the other hand, small vessels in subjects with sustained hypertension have a higher vascular resistance but are less distensible than those in normotensive subjects at the same TMP. One can speculate regarding the importance of these findings during the development, maintenance, and regression of
hypertension. For example, if in the initial stages of the disease, small vessels behave as the normal contracted vessels (Figure 2) and, as the disease process advances (and structural changes take place in the vascular wall), if the behavior changes to that shown in Figure 1 for hypertensives, then we may be able to gain insight into the sequence of events that occurs in the vessel wall as the disease progresses.12

In conclusion, we have described a theoretical method to calculate distensibility of maximally dilated small blood vessels (resistance vessels) from noninvasively obtained pressure-flow data in humans. This method is more direct and more accurate than the one previously reported2 and provides an instantaneous value of E that, unlike the previous method, does not require a linear fit to the plot of ln G1/4 versus TMP. The method should prove useful for evaluating the status of small blood vessels, at specified intervals, in patients with hypertension or other small vessel diseases in an outpatient setting.

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References


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