Effective diameter as a determinant of local vascular resistance in presence of vasomotion

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SLAAF, DICK W., HUUB H. E. OUDE VRIELINK, GEERT-JAN TANGELDER, AND ROBERT S. RENEMAN. *Effective diameter as a determinant of local vascular resistance in presence of vasomotion.* Am. J. Physiol. 255 (Heart Circ. Physiol. 24): H1240–H1243, 1988.—The mean resistance of arterioles exhibiting rhythmic changes in diameter (vasomotion) depends on the mean vascular diameter and the amplitude and shape of the vasomotion pattern. The effective diameter, defined as the diameter of a tube with constant diameter and the same vascular resistance as the vessel showing vasomotion, was calculated using Poiseuille's law. The effective diameter was used to compare the results of model calculations of square wave, sinusoidal, and triangular vasomotion patterns with those obtained from rabbit tenuissimus muscle arterioles. Due to the variability of the actual vasomotion waveforms, approximation of the effective diameter using the mean diameter, the relative vasomotion amplitude, and an assumed waveform led to erroneous results. Therefore, effective diameter should be calculated directly from the actual arteriolar diameter tracings to take into account all irregularities in the vasomotion pattern.

flow; microcirculation; hindrance; Poiseuille's law

IN RESTING TISSUES the arteriolar diameter often varies with time in a cyclic way (vasomotion) and causes vascular resistance to be time dependent. When only geometrical factors are considered, mean vascular resistance, defined as the temporal mean of the resistance over one vasomotion cycle, depends not only on mean vascular diameter and vasomotion amplitude (3) but also on the pattern of vasomotion. Vasomotion cycle length per se does not influence mean vascular resistance (3) unless there is also a change in the pattern of vasomotion. The suggestion that vasomotion lowers vascular resistance, as compared with that of a vessel with the same mean diameter but without vasomotion, is correct but misleading. This would indicate that in a certain physiological state mean vascular diameter rather than flow is regulated. However, it is more likely that an organ receives the same amount of flow whether or not its arterioles show vasomotion. Hence, reference should be made to the diameter value indicative of the flow-carrying capacity of the vessel.

The complicated interplay between the different vasomotion parameters (amplitude, rate of dilation or constriction, and shape) make it difficult to appreciate in a direct, unambiguous way the extent of their influence on vascular resistance. To avoid this problem, it is proposed to calculate from the actual diameter tracings the effective diameter (D_{eff}), defined as the diameter of a tube with constant diameter, and the same vascular resistance as the vessel showing vasomotion. Model calculations were performed for square wave, sinusoidal, and triangular vasomotion patterns, and the results obtained were compared with those obtained from vasomotion patterns in rabbit tenuissimus muscle arterioles (4).

METHODS

Principle. To calculate the contribution of vasomotion to the resistance and flow-carrying capacity of a microvessel, cylindrical vessel segments of equal length and uniform diameter were compared. With the use of Poiseuille's law and the assumption that the rheological properties of blood are constant, flow as an instantaneous function of time [$\dot{Q}(t)$] is proportional to $D^4(t)$, where $D(t)$ is the instantaneous vessel diameter, and t is time (1). For a constant pressure gradient (ΔP) along the vessel segment, mean blood flow can be computed from

$$\bar{\dot{Q}} = \alpha \int_0^T D^4(t)dt \Big/ \int_0^T dt \qquad (1)$$

where T is vasomotion cycle length, and α is a proportionality factor.

D_{eff}, defined as the diameter of a tube with uniform constant diameter without vasomotion and the same flow-carrying capacity as the vessel showing vasomotion, was calculated from $\bar{\dot{Q}} = \alpha D_{eff}^4$, yielding

$$D_{eff} = \left[\int_0^T D^4(t)dt \Big/ T \right]^{1/4} \qquad (2)$$

With the use of this equation, D_{eff} was calculated from actual in vivo tracings (Fig. 1) obtained from experiments similar to those performed before (4). The diameter data were digitized at a sampling rate of 12.5 Hz using a 12-bit analog-to-digital converter and were stored on floppy disk. Computations were performed on a Digital, Minc-11 computer. The integration process of the digitized data was performed by summing the fourth power of each sample point and dividing the result by the number of samples (N)

$$D_{eff} = \left(\sum_{i=1}^{N} D_i^4 \Big/ N \right)^{1/4} \quad (3)$$

The integration process was performed over an integer number of vasomotion cycles. Because at least four vasomotion cycles were taken and the sampling frequency of 12.5 Hz is much higher than the vasomotion frequency (0.2–0.5 Hz), the error can be estimated to be far less than 1%.

Defining vascular hindrance (H), by taking into account only the geometrical factors of resistance, mean vascular hindrance ($\bar{H}$) over one vasomotion cycle is inversely proportional to mean flow (1): $\bar{H} \cong 1/\bar{Q}$. The ratio of hindrance of two vessels with different effective diameters can be calculated according to

$$\bar{H}_1/\bar{H}_2 = (D_{eff_2}/D_{eff_1})^4 \quad (4)$$

Model calculation of D_{eff} for different vasomotion patterns. $D(t)$ consists of a constant part D and a time-dependent part $A(t)$, i.e., $D(t) = D + A(t)$. The peak-to-peak difference of the time-dependent part $A(t)$ is A. D_{eff} is calculated using *Eq. 2.* Integration was performed analytically over one vasomotion cycle using the equations of the waveforms as given in APPENDIX.

Square wave vasomotion. In this case (Fig. 2*A*) it holds

$$D_{eff}^4(\mathrm{Sq}, b, D, A) = b(D + \tfrac{1}{2}A)^4 + (1 - b)(D - \tfrac{1}{2}A)^4 \quad (5)$$

Coefficient b describes the fraction of time spent in the dilated state and Sq represents square wave. Only if $b = 0.5$ does it hold that $\bar{D}$ (mean vascular diameter over one vasomotion cycle) equals D.

In this approach the result obtained is independent of the cycle length. However, if the vasomotion cycle length is changed by adding to each initial vasomotion cycle a fractional period aT (Fig. 2*D*), during which the vessel remains in the vasodilated state ($D + \frac{1}{2}A$), the following relation has to be used

$$D_{eff}^4(\mathrm{Sq}, b, D, A, a) = [(b + a)(D + \tfrac{1}{2}A)^4 + (1 - b)(D - \tfrac{1}{2}A)^4]/(1 + a) \quad (6)$$

where a defines the fractional period.

Triangular shape of vasomotion (Fig. 2, B and E). In this situation the result is independent of the actual shape of the triangle (Tr)

$$D_{eff}^4(\mathrm{Tr}, c, D, A, a) = [(D + \tfrac{1}{2}A)^5 - (D - \tfrac{1}{2}A)^5 + 5aA(D + \tfrac{1}{2}A)^4]/5A(1 + a) \quad (7)$$

Coefficient c, proportional to the steepness of the rise (cT/A) (Fig. 2*B*), does not appear in the results. If $a = 0$ it holds that $\bar{D} = D$.

Sinusoidal shape of vasomotion (Fig. 2, C and F). In this situation the result is given by

$$D_{eff}^4(\mathrm{Si}, D, A, a) = D^4\left[1 + a + 2a\left(\frac{A}{D}\right) + \left(\frac{3}{4} + \frac{6a}{4}\right)\cdot\left(\frac{A}{D}\right)^2 + \frac{1}{2}a\left(\frac{A}{D}\right)^3 + \frac{3 + 8a}{128}\left(\frac{A}{D}\right)^4\right] \Big/ (1 + a) \quad (8)$$

Again if $a = 0$ it holds that $\bar{D} = D$ (Fig. 2, *C* and *F*).

Data presentation. For convenience of interpretation, the data presented in Figures 3 and 4 are normalized: D_{eff} to D and vasomotion amplitude to $2D$.

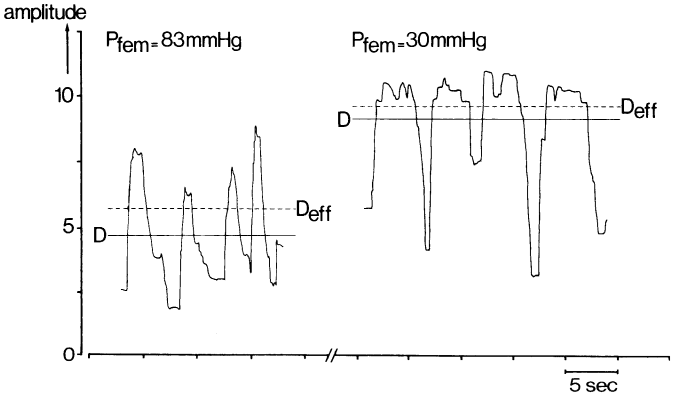

FIG. 1. Vasomotion pattern of terminal arteriole of rabbit tenuissimus muscle at 2 different perfusion pressure levels (P_{fem}). D, diameter; D_{eff}, effective diameter.

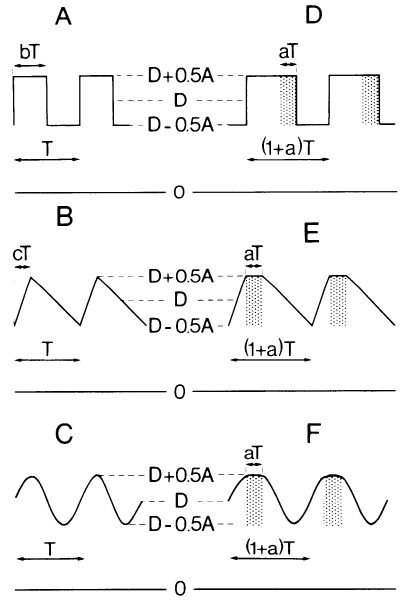

FIG. 2. Schematic representation of 3 vasomotion patterns. *A*: square-wave; coefficient b denotes fraction of time spent in vasodilated state. *B*: triangular pattern; coefficient c denotes fraction of time spent in vasodilating state. *C*: sinusoidal wave pattern. In *D*, *E*, and *F* vasomotion cycle length is increased by a fractional period aT, during which vessel remains in vasodilated state (□).

RESULTS AND DISCUSSION

Superposition of a symmetric vasomotion pattern on a constant diameter D leads to an increase in D_{eff} and a concomitant decrease in H. In Fig. 3 the relative effective diameters are plotted as a function of the relative vasomotion amplitude ($A/2D$) for the three different patterns of vasomotion: a symmetric square wave ($b = 0.5$) and a sinusoidal and a triangular pattern. The straight line indicates the increase of D_{eff} for a tube with uniform constant diameter $D + \frac{1}{2}A$, which represents the upper bound of the effect of vasomotion on the effective diameter.

Consider the case of a square wave with $A = 2D$, which means that during the vasomotion cycle the vascular lumen completely closes, as frequently occurs in terminal arterioles of the rabbit tenuissimus muscle. In this case $D_{eff} = 2D\sqrt{b}$ (see *Eq. 5*). Therefore, if the terminal arteriole is open to flow at a diameter of $2D$ during only 6.25% [$= (0.5)^4 \cdot 100\%$] of the vasomotion cycle, then it has the same resistance to flow as a vessel with constant diameter D. This is indicated by the fact that in both cases $D_{eff} = D$, although in the former case, the mean diameter is only $0.125D$. If the terminal arteriole is open (at $2D$) during 50% of the vasomotion cycle ($b = 0.5$), then D_{eff} reaches a value of $1.68D$. If in this case vasomotion ceases and the diameter becomes constant at $2D$, then the hindrance is only reduced by a factor of 2. In case of a sinusoidal or triangular vasomotion pattern with complete closure during part of the cycle, cessation of vasomotion, resulting in a constant diameter of $2D$, reduces H by a factor of 3.7 and 5.0, respectively.

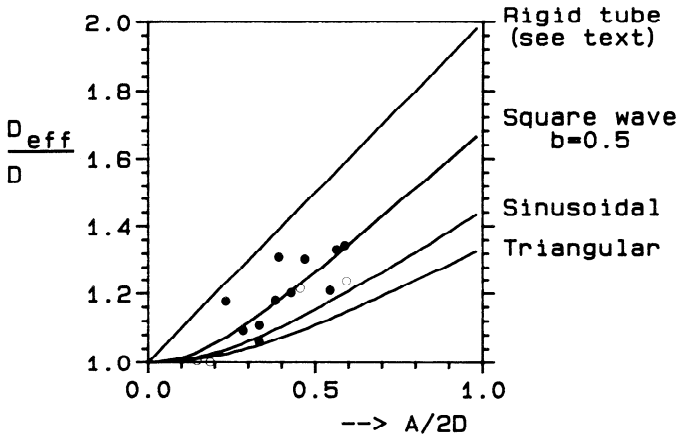

FIG. 3. Normalized effective diameter (D_{eff}) as a function of relative vasomotion amplitude (A). Straight line depicts D_{eff} of a rigid tube with a diameter $D + \frac{1}{2}A$. Data calculated from in vivo tracings from transverse (○) and terminal (●) arterioles are indicated.

An increase in vasomotion cycle length by adding a fractional period (aT), during which the vessel remains in the vasodilated state ($2D$), leads to an increase of D_{eff}, as is shown in Fig. 4. This increase is most pronounced for the pattern with initially the smallest influence on D_{eff} (the triangle). In the range of relative cycle length changes, as observed in the rabbit tenuissimus muscle during reduction of perfusion pressure ($a \leq 0.4$), D_{eff} becomes maximally $1.79D$, $1.67D$, and $1.62D$ [square wave ($b = 0.5$), sinusoidal, and triangular pattern, respectively]. This means a reduction of H by a factor of 1.29, 1.76, and 2.13, respectively.

In transverse arterioles of rabbit tenuissimus muscle, the vasomotion amplitude hardly exceeds $0.5D$. The effective diameters for a vessel with a vasomotion amplitude of $0.5D$ are $1.08D$, $1.04D$, and $1.03D$ (square wave, sinusoidal, and triangular pattern, respectively). An increase in vasomotion cycle length by 40% at a diameter equal to the maximum during the vasomotion cycle ($1.5D$) would increase D_{eff} to $1.14D$, $1.12D$, and $1.11D$, respectively. The significance of these relatively small changes in diameter becomes evident when the fourth power of the diameter is taken to calculate the relative hindrance. A D_{eff} of $1.08D$ and $1.14D$ implies a relative hindrance of 0.74 and 0.59, respectively. Although this effect is considerable, it is still limited when compared with that of a dilation to a constant diameter of $1.5D$, the maximal diameter during vasomotion. In this case the relative hindrance would be reduced to 0.20.

The use of the entity "effective diameter" also eliminates complications when two factors are opposing. It is difficult to appreciate in a direct, unambiguous way whether a vessel with a mean diameter of 25 μm and with a sinusoidal vasomotion pattern with a peak-to-peak amplitude of 5 μm has a higher or a lower hindrance than a vessel with a mean diameter of 22 μm and a vasomotion amplitude of 22 μm. Comparison of their effective diameters, however, yields that these are virtually the same (25.2 and 25.4 μm, respectively), thus

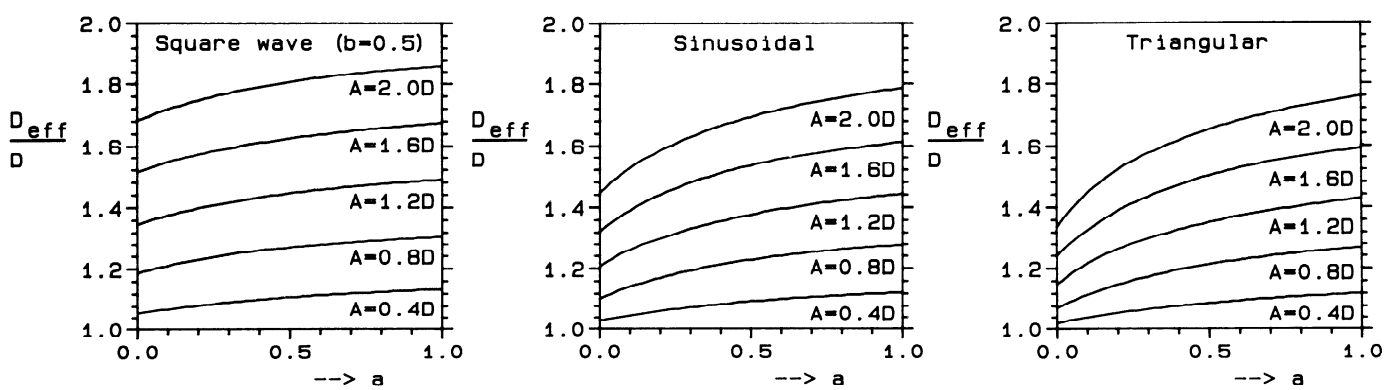

FIG. 4. Normalized D_{eff} as a function of coefficient a for different vasomotion amplitudes (A) superimposed on a constant diameter D. Coefficient a determines increase in cycle length by fractional period aT, which is spent in vasodilated state ($D + \frac{1}{2}A$).

indicating that the vessels have the same mean hindrance and flow-carrying capacity.

The scatter of the in vivo data shown in Fig. 3 demonstrates that the patterns cannot be approximated by a mean diameter, a vasomotion amplitude, and one type of pattern. The model calculations are based on symmetric vasomotion patterns, whereas in vivo the vasomotion patterns are often asymmetric. The actual mean vessel diameter is considerably less than that calculated as the mean of the highest and lowest values during vasomotion. Corrections for this asymmetry are less relevant, since shape changes can still have a considerable influence as is shown by the model calculations.

In the present study the rheological factors have been assumed to be constant through the vasomotion cycle. However, the relative hematocrit in capillaries and terminal arterioles varies during the vasomotion cycle (2). To what extent this influences the viscosity is still unclear. Inclusion of these aspects in the model requires simultaneous measurement of changes in arteriolar diameter and hematocrit, which is difficult in skeletal muscle preparations. Besides, it is unknown whether there is a good relation between relative hematocrit and viscosity.

In conclusion, the effective diameter of a microvessel showing vasomotion provides direct insight into the vascular resistance or flow-carrying capacity of that vessel. The effective diameter should be calculated directly from the actual arteriolar diameter tracings, to take into account all irregularities in the vasomotion pattern.

APPENDIX

Equations of waveforms are shown in Fig. 2.

Square wave vasomotion (Fig. 2, A and D)

$$D(t) = D + 0.5A \quad \text{if} \quad 0 < t < (b + a)T$$

$$D(t) = D - 0.5A \quad \text{if} \quad (b + a)T < t < (1 + a)T$$

$$0 \leqq A \leqq 2D \qquad 0 \leqq b \leqq 1 \qquad a \geqq 0$$

Triangular shape of vasomotion (Fig. 2, B and E)

$$D(t) = D - 0.5A + \frac{A}{cT} \cdot t \quad \text{if} \quad 0 \leqq t \leqq cT$$

$$D(t) = D + 0.5A \quad \text{if} \quad cT \leqq t \leq (a + c)T$$

$$D(t) = D + 0.5A - \frac{A}{(1 - c)T} \cdot [t - (a + c)T]$$

$$\text{if} \quad (a + c)T \leqq t \leqq (1 + a)T$$

$$0 \leqq A \leqq 2D \qquad 0 \leqq c \leqq T \qquad a \geqq 0$$

Sinusoidal shape of vasomotion (Fig. 2, C and F)

$$D(t) = D + 0.5A \sin t \quad \text{if} \quad 0 \leqq t \leqq \tfrac{1}{4}T$$

$$D(t) = D + 0.5A \quad \text{if} \quad \tfrac{1}{4}T \leqq t \leqq (\tfrac{1}{4} + a)T$$

$$D(t) = D + 0.5A \sin(t - aT) \quad \text{if} \quad (\tfrac{1}{4} + a)T \leqq t \leqq (1 + a)T$$

$$T = 2\pi$$

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REFERENCES

1. BURTON, A. C. *Physiology and Biophysics of the Circulation.* Chicago, IL: Year Book, 1962.
2. FAGRELL, B., M. INTAGLIETTA, AND J. ÖSTERGREN. Relative hematocrit in human skin capillaries and its relation to capillary blood flow velocity. *Microvasc. Res.* 20: 327–335, 1980.
3. FUNK, W., B. ENDRICH, K. MESSMER, AND M. INTAGLIETTA. Spontaneous arteriolar vasomotion as a determinant of peripheral vascular resistance. *Int. J. Microcirc. Clin. Exp.* 2: 11–25, 1983.
4. SLAAF, D. W., G. J. TANGELDER, H. C. TEIRLINCK, AND R. S. RENEMAN. Arteriolar vasomotion and arterial pressure reduction in rabbit tenuissimus muscle. *Microvasc. Res.* 33: 71–80, 1987.