Nonuniform Vasomotor Responses of the Coronary Microcirculation to Serotonin and Vasopressin

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Large-conduit coronary arteries respond to vasoactive stimuli differently than smaller coronary arterioles, but the quantitative effects of many vasoactive stimuli at various levels of the microvasculature remain unknown. To determine the site of constriction or dilation to serotonin and vasopressin in the coronary microcirculation, we studied microvascular responses in the left ventricle of anesthetized cats (n = 36). To compensate for motion due to contraction of the heart, the epicardium was visualized with stroboscopic epi-illumination controlled by a computer to flash once per cardiac cycle in mid-diastole, making the vessels appear stationary. Serotonin (16 μg/kg/min) or vasopressin (0.5 units/min) was infused into the left atrium while maintaining aortic pressure constant with a snare on the descending aorta or inferior vena cava. Myocardial blood flow was measured with radioactive microspheres. During infusion of serotonin, aortic pressure and heart rate did not change, but myocardial perfusion increased 90±38% (mean±SEM) from a control value of 159±27 ml/min • 100 g. Arteries and arterioles larger than 90 μm constricted in response to serotonin (control 159±12 μm; percent change -18±3; range -41 to 10%) while arterioles less than 90 μm dilated to serotonin (control 54±7 μm; percent change 22±9; range -10 to 62%). During infusion of vasopressin, aortic pressure and heart rate did not change, and myocardial perfusion decreased 16±7% (control, 147±18 ml/min • 100 g). In contrast to serotonin, infusion of vasopressin constricted arterioles less than 90 μm (control, 55±5 μm; percent change -16±3; range -27 to -2%) while arteries and arterioles larger than 90 μm did not respond or dilated modestly (control, 190±11 μm; percent change 4±2; range -29 to 43%). These responses to serotonin and vasopressin suggest that vasomotor regulatory mechanisms vary in different size arteries and arterioles in the coronary microcirculation, and the pivotal size at which differential changes occur is the 90-μm level.

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Previous studies of the coronary microcirculation have been hampered by the inability to visualize arterioles because of respiratory and cardiac-induced motion of the heart. Techniques that have been used to study segmental coronary vascular resistance include measurements of pressure gradients and measurements of large arterial versus arteriolar resistance with sonomicroscopy and myocardial perfusion, respectively.1-3 Neither of these techniques, however, can be used to identify physiological responses of specific arteriolar segments in the microcirculation.

Recently, two techniques have been developed to minimize or compensate for cardiac and respiratory-induced motion and allow direct visualization of the microcirculation with minimal trauma to the heart.4,5 The first technique minimizes respiratory-induced motion of the heart by ventilating animals with high-frequency ventilation synchronized to the cardiac cycle. Because tidal volume is small, there is little respiratory effect on cardiac motion. The second technique compensates for motion due to contraction of the heart by illuminating the epicardium with a computer-controlled stroboscopic light source. Stroboscopic illumination is synchronized to flash at the same point during each cardiac cycle.
over-the-needle catheter was inserted into the trachea distal to the tracheal cannula and advanced to the trachea carina. Compressed air (5–7 psi) was injected into the trachea through the intracatheter by a solenoid valve, which was triggered off the first positive slope of left ventricular dP/dt. The solenoid valve was open 15–20 msec per cardiac cycle. The tracheal cannula was placed under 1–3 cm of water to maintain positive end-expiratory pressure. By use of this system, respiration was synchronized with the cardiac cycle, and tidal volume during pulmonary inflation was small; therefore, there was little effect of respiration on cardiac motion. In addition, cardiac filling pressures were held constant, minimizing respiratory-induced changes in arterial pressure and stroke volume. The arterial blood gases were maintained within physiological ranges by varying the duration of the inflation, the position of the intracatheter in the trachea, the pressure of the air injected into the trachea, and positive end-expiratory pressure.

Microscope and Illumination Systems

The left ventricle was positioned under a vertically mounted Leitz Ploemopak microscope system. The table beneath the microscope could be moved in an x-y plane that enabled visualization of multiple fields of microvessels in a single preparation. The epicardial surface of the heart was epi-illuminated with a xenon arc stroboscopic light source (Chadwick Helmuth, El Monte, California) and the Leitz Ploemopak. Leitz A6 and Leitz L10 (n.a. 0.18 and 0.22) microscope objectives were used with a ×10 eyepiece. Despite high-frequency ventilation and stroboscopic illumination, the myocardial surface was not at the same point in each cardiac cycle. Therefore, higher-power objectives (×20) were not used for obtaining images of microvessels because the focal depth of the ×20 objective was very shallow.

The microvascular field in each study was illuminated at a single point in mid-diastole during each cardiac cycle. A PDP 11/73 microcomputer controlled triggering of the strobe from left ventricular dP/dt using the first positive slope of dP/dt as the initial trigger point. The delay between the initial trigger point and the strobe flash (15–25 μsec) was adjusted so that visualization of the microcirculation occurred in mid-diastole.

Differentiation of microvascular arteries and veins was accomplished by viewing the sequence of illumination of vessels after injection of fluorescein-labeled dextran (fluorescein isothiocyanate dextran, 150,000 Da, 50 mg/ml in 0.9% saline) injected into the left atrial appendage and viewed with a Leitz fluorescent filter. With this technique, the arterial circulation fluoresced first; later, the venous circulation was illuminated.
Measurements of Microvascular Diameters

Microvascular diameters were measured with a silicon-intensified tube video camera (General Electric, Owensboro, Kentucky) and a video digitizer (Imaging Technology, Woburn, Massachusetts). The video camera was optically coupled to the intravital microscope. With stroboscopic illumination, the microvessels appeared stationary, and images were digitized and displayed on a high-resolution monitor. Microvessels were viewed, and selected images during each intervention were stored in the computer for later analysis. The monitor screen was calibrated by projecting a micrometer grid in the microscope field. Microvascular diameters were measured with a digitizing tablet (Summa Graphics, Cambridge, Massachusetts) from the ratio of micrometer length/video length. The pixel size of the digitized images was 4.6 μm with the ×6 objective and 2.6 μm with the ×10 objective. Arteriolar diameters were measured as the distance between a selected point on the luminal wall and the nearest point on the opposite wall. Since a comparison of microvascular diameters before and after each intervention necessitated measurements of vessels at the same place in the microvasculature, anatomical landmarks such as branch points or crossing vessels were used to identify particular vascular locations. A minimum of four different images was used to measure a particular microvessel, and the arithmetic mean was used to calculate average size for each vessel.

Myocardial Blood Flow

Myocardial perfusion was measured with the radioactive microsphere technique. Microspheres (1×10⁴, 15-μm diameter) labeled with ⁴⁶Sc, ⁸⁵Sr, ⁶⁵Zn, ⁶⁷Cu, ⁶⁹Ga, ⁷⁵Se, ⁷⁶As, ⁸ⁱmKr, ⁸⁵Rb, ⁹⁰Y, ⁹⁵Zr, ⁹⁶Nb, or ⁹⁹mTc were vortexed for a minimum of 5 minutes and injected into the left atrial appendage followed by a saline flush. Before and for 1.5 minutes after microsphere injection, a reference flow sample was withdrawn from the femoral artery at a constant rate. Tissue and reference samples were counted in a Canberra Germanium crystal gamma counter (Meriden, Connecticut), and myocardial blood flow (MBF) was calculated using the equation:

\[
MBF (\text{ml/min} \cdot \text{g}) = \frac{\text{CM} (\text{counts/time} \cdot \text{g}) \times W (\text{ml/min})}{\text{CR (counts/time)}},
\]

where CM is sample counts, W is withdrawal rate of the pump, and CR is reference blood-flow counts. Myocardial blood flow was expressed as the mean of all samples in each study.

Validation of Microvascular Diameter Measurements

Since the results of these studies are dependent on the precision and reproducibility of our diameter measurements, studies were undertaken to measure the spatial resolution of our system, the interobserver variability, and the effect of plasma skimming on the measurement of microvascular diameters. The spatial resolution of the digitized imaging system was measured by comparing measurements of latex beads from 5 to 35 μm measured with a ×20 objective, which we defined as absolute diameter to measurements made with the ×6 and ×10 objectives used in these studies.

Since these studies are dependent on observer measurement of vessel diameter, the degree of variability in the data may be related to interobserver measurement. This interobserver variability was determined by comparing measurements of the same artery or arteriole by two independent observers.

The third factor that may have increased the variability within the data is the effect of plasma skimming on the measurement of diameter. Measurement of microvascular diameters with images obtained with polarized light allows measurements of the column of red blood cells within the vessel. However, when vessels are illuminated with fluorescein-labeled dextran, the entire vessel lumen including the plasma layer can be measured. If plasma skimming is a significant factor in these microvessels, the difference between measurements made with polarized light and fluorescein-labeled dextran would be important. Therefore, in nine dogs instrumented similarly, over a wide range of vessel sizes, measurements of arterial diameters made with polarized light were compared with measurements of the same arteriole made with fluorescent images.

Protocol

In a series of preliminary experiments, serotonin (4–16 μg/kg/min) or vasopressin (0.1–0.5 units/min) was infused, and microvascular diameters were measured at each dose. Consistent changes in arteriolar diameters were observed at 16 μg/kg/min of serotonin and 0.5 units/min of vasopressin. Therefore, these doses of drugs were used in this study. Control measurements of microvascular diameter, hemodynamics, and myocardial perfusion were obtained before infusion of either agent. Serotonin (n=12, 16 μg/kg/min) or vasopressin (n=24, 0.5 units/min) was infused into the left atrial appendage. Changes in aortic pressure were prevented during infusion of serotonin or vasopressin by tightening a snare of umbilical tape around the descending aorta or inferior vena cava. Myocardial perfusion was measured with the radioactive microsphere technique in eight of the 12 cats given serotonin and 12 of the 24 cats given vasopressin. After 5 minutes of drug infusion, microvascular diameters and hemodynamics were measured. No animal received more than one agent although all but nine cats received a lower dose of each agent. The number of vessels measured per animal varied from one to seven and averaged 2.5±0.3 vessels per cat.
Criteria for an Acceptable Experiment
Animals were excluded from the study if the mean arterial pressure was less than 60 mm Hg. Arterial blood gases had to be within the physiological range (pH 7.35-7.45, Pco2 25-40 mm Hg, and Po2 80-125 mm Hg), and mean arterial pressure during an intervention had to be maintained within 10 mm Hg of the control level.

Statistical Analysis
Total coronary vascular resistance was calculated as mean arterial pressure divided by myocardial blood flow. Changes in microvascular resistance were estimated as a percent change in hindrance. Hindrance changes are an index of resistance changes since they do not include measurements of either segment length or viscosity. A percent change in hindrance was calculated as

\[ \% \Delta H = \frac{1/r_d^4 - 1/r_c^4}{1/r_c^4} \times 100 \]

where \( H \) is hindrance, \( r_d \) is radius of arteriole during intervention, and \( r_c \) is radius of arteriole at control.

All data are expressed as mean±SEM. Hemodynamic measurements, myocardial perfusion data, and percent change in vessel diameter were analyzed with Student's \( t \) test for paired comparison. Significance was accepted at the \( p<0.05 \) level.

Results
Validation Studies—Spatial Resolution
Figure 1 illustrates the comparison of measurement of absolute bead diameter (×20 objective) versus measurement of the same latex beads with the ×6 and ×10 objectives coupled with our digital imaging system. With the ×6 objective, the relation between absolute diameter and the measured diameter was linear down to approximately 9 μm. Measurement of latex beads less than 8 μm with the ×6 objective tended to overestimate the actual bead diameter. With the ×10 objective, the relation between measured diameter and absolute diameter was linear to approximately 5 μm.

Interobserver Variability
Figure 2 illustrates the results of a comparison of measurements of arteriolar diameters by two different observers. There was a high correlation between the two measurements (slope 0.98) with a y-intercept of 3.4 μm. The standard error of the estimate was 0.4 μm and indicated very little interobserver variability.

Polarized Light Versus Fluorescent Images
Figure 3 illustrates the relation between measurements of arteriolar diameters with polarized light and measurements of arteriolar diameters with fluorescent images. The measurements made of the same vessel with these two different methods of illumination showed a good correlation.

Serotonin
Hemodynamics. During infusion of serotonin, mean aortic pressure was held constant with a snare on the descending aorta (Table 1). Heart rate was
not altered. The effect of serotonin (16 μg/kg/min) on myocardial perfusion to the left ventricle was measured in eight of the 12 cats (Figure 4). Myocardial perfusion increased 91 ±38% from a control value of 159 ±27 ml/min/100 g.

**Microvascular diameters.** The relation between arteriolar diameter and the percent change in diameter from control in response to serotonin is illustrated in Figure 5. Arterioles less than 90 μm dilated in response to serotonin (control 54 ±7 μm, percent change 22 ±9) (Figure 6). Conversely, arteries and arterioles greater than 90 μm constricted (control 159 ±12 μm, percent change -18 ±3).

**Change in hindrance.** During infusion of serotonin, total coronary vascular resistance decreased by 34 ±12% (control 0.70 ±0.07 mm Hg×ml/100 g/min; Figure 4B). However, when the hindrance of the arteriolar segments was calculated, a heterogeneous response was observed (Figure 7). Hindrance increased in the larger arteries and arterioles and decreased in the smallest arterioles.

**Table 1. Aortic Pressure and Heart Rate During Infusion of Serotonin**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Serotonin (16 μg/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pressure (mm Hg)</td>
<td>124 ±8</td>
<td>129 ±7</td>
</tr>
<tr>
<td>Diastolic pressure (mm Hg)</td>
<td>92 ±8</td>
<td>85 ±10</td>
</tr>
<tr>
<td>Mean pressure (mm Hg)</td>
<td>104 ±8</td>
<td>106 ±7</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>184 ±8</td>
<td>197 ±6</td>
</tr>
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</table>

Values are mean ±SEM; n = 12.
Microvascular diameters. Arterioles below 90 μm constricted in response to vasopressin (control 55±5 μm, percent change -16±3) (Figure 6). Although there was greater variability in the response of arteries and arterioles greater than 90 μm to vasopressin, vasopressin resulted in modest dilation when compared with control (control 190±11 μm, percent change, 4±2) (Figure 6). The relation between responses of the coronary arteriolar microcirculation to vasopressin and vessel size is illustrated in Figure 8.

Change in hindrance. During infusion of vasopressin, total coronary vascular resistance increased by 31±10% (control 0.76±0.08 mm Hg×ml×100 g/min, Figure 4B). The percent change in hindrance compared with arteriolar size was heterogeneous (Figure 9). Hindrance was increased in smaller arterioles; however, there was a minimal change in larger arterioles and arteries.

Discussion

These studies demonstrate that responses of the coronary microvasculature to the humoral agents serotonin and vasopressin are markedly different depending on the size of the arteriolar segment. Specifically, coronary arterioles less than 90 μm dilate to serotonin whereas arteries and arterioles greater than 90 μm constrict. Arterioles less than 90 μm constrict to vasopressin whereas arteries and arterioles greater than 90 μm do not respond or dilate minimally to vasopressin. Thus, the coronary microvasculature responds in a remarkably heterogeneous manner to serotonin and vasopressin.

Validation of Diameter Measurements

Since diameter responses to serotonin and vasopressin throughout the microvasculature are dependent upon the reliability and accuracy of our measurements, we examined three variables that could have influenced these results. First, the spatial resolution of the digitized images was measured by comparing diameter measurements of latex beads. In our system, pixel size of the digitizing system is 4.6 μm with the ×6 objective and 2.6 μm with the ×10 objective. In this static system, the spatial resolution of the digitized images was measured by comparing diameter measurements of latex beads.
Several mechanisms may be proposed to explain the differential responsiveness of vascular diameters under the conditions of these studies. First, there may be a different receptor population in the different sized arteries versus arterioles. Second, the role of the endothelium in modulating responses of different sized arterioles either directly or indirectly through changes in coronary flow may vary with vessel size. Third, autoregulatory adjustments may occur in large and small arterioles to maintain normal coronary vascular resistance. Finally, indirect effects of serotonin and vasopressin may vary in different sized arterioles and may contribute to the heterogeneous responses observed. These possible mechanisms will be discussed separately.

**Differential receptor populations.** Studies in cremaster muscle and the coronary circulation suggest that the differential responses to serotonin are a result of different receptor populations in large versus small arteries. In the coronary circulation, selective blockade of 5-HT1 receptors prevented constriction of large artery responses, but increases in coronary blood flow to serotonin were not altered. Conversely, dilation of small arterioles (<50 μm) in rat cremaster muscle appears to be mediated by a 5-HT1 receptor subtype.

In other vascular beds such as the mesentery, the vascular response to vasopressin varies with the vascular segment decreasing from venule to capillary to metarteriole to arteriole. The mechanism responsible for these varying responses is not entirely clear but may involve different receptor populations. Presently, at least two distinct receptor populations for vasopressin have been identified. One receptor (V1) is generally considered to mediate vasoconstriction, and the other (V2) mediates the antidiuretic activity of vasopressin and vasodilation in some vessels.

Thus, it is possible that the ratio of these receptor subtypes for serotonin and vasopressin may vary with vascular size. Under such conditions, the net response of a given vascular segment would be determined by the predominant receptor subtype present and could vary from dilation to constriction.

**Role of endothelium in responses of vascular smooth muscle.** Since the observations of Furchgott and Zawadzki in 1980 of the role of endothelium in modulating responses of vascular smooth muscle to acetylcholine, vascular responses to a wide variety of substances including serotonin and vasopressin have been shown to be influenced by the presence of an intact endothelial layer both in vitro and in vivo. In addition to a direct effect of humoral substances on endothelium to release an endothelium derived relaxing factor(s) (EDRF), physiological stimuli such as an increase in blood flow can also stimulate the endothelium to release EDRF. Although endothelium can modulate responses of large coronary arteries to serotonin and vasopressin, its role in vascular responses at the microvascular level is not as well defined. Also, if endothelium does modulate responses in the micro-

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**Figure 9.** Plot showing relation between control arterial or arteriolar diameter and percent change in hindrance (% ΔH) in response to vasopressin (0.5 units/min).

Resolution was approximately 9 μm for the x6 objective and approximately 5 μm for the x10 objective. These data are consistent with the established concept that the spatial resolution of measurements of digitized images is the distance of two pixels.

Second, when a predetermined vascular site was measured by two independent observers, the correlation between measurements was very good. Thus, the results of this study could not be adversely influenced by interobserver variability in the measurement of arteriolar diameter.

A third factor that could have influenced our diameter measurements is the thickness of the plasma layer in each arteriole. When measurements of arteriolar diameters are made with polarized light, the diameter measurement is a measure of the column of red blood cells within the vessel. The thin layer of plasma along the vessel wall is not included in the diameter measurement. The inability to measure this plasma layer with polarized light may have greater influence on the accuracy of measurements of smaller arterioles. However, over a wide range of vessel sizes, we found that there was a good correlation between diameter measurements made with polarized light versus fluorescent light. Therefore, failure to include the width of the plasma layer in the measurement of arteriolar diameter would have little effect on the results of this study. Thus, diameter measurements of arterioles with polarized light are an accurate measurement of actual microvascular diameters under the conditions of these studies.

These three validation studies indicate that images of coronary microvessels in our system either polarized or fluorescent light can be used to measure changes in vessel diameter with precision and reproducibility in the 5-μm range.

**Mechanisms of Differential Responses of Coronary Microcirculation**

At least four different mechanisms may be proposed to explain the differential responsiveness of various segments in the coronary microcirculation to serotonin and vasopressin. First, there may be a different receptor population in the different sized arteries versus arterioles. Second, the role of the endothelium in modulating responses of different sized arterioles either directly or indirectly through changes in coronary flow may vary with vessel size. Third, autoregulatory adjustments may occur in large and small arterioles to maintain normal coronary vascular resistance. Finally, indirect effects of serotonin and vasopressin may vary in different sized arterioles and may contribute to the heterogeneous responses observed. These possible mechanisms will be discussed separately.
circulation, it is also possible that the amount of EDRF released may vary with vessel size.

Studies examining the role of endothelium in the microcirculation have demonstrated that responses to humoral agents in arterioles may not be the same as that observed in large arteries. For example, in skeletal muscle, blockade of EDRF with methylene blue26 or hydroquinone27 prevented arteriolar dilation in response to acetylcholine but not to serotonin.27 This finding suggests that at least in skeletal muscle, serotonin does not cause release of EDRF in small arterioles. The ability of acetylcholine to release EDRF also appears to vary with vessel size, at least in rabbit ear artery in which arterioles around 75 μm were more sensitive to the dilatory effects of acetylcholine than arteries and arterioles from 150 to 300 μm.28

The role of endothelium in the microcirculation also varies markedly between different vascular beds. In the cerebral circulation, damage to endothelium can prevent dilation to acetylcholine29,30 whereas in hamster cheek pouch, there is no evidence for endothelium-dependent vasodilation to acetylcholine.31 Flow-mediated dilation also occurs in the microcirculation of various vascular beds since it has been demonstrated in the mesentery32,33 and cremaster muscle.34 Recent evidence has suggested that endothelium can modulate responses to acetylcholine in the coronary circulation in 50–150 μm arterioles since dilation of small coronary arterioles in vitro in response to acetylcholine could be prevented by free hemoglobin that specifically binds EDRF.35

Although the potential importance of direct or flow-mediated release of endothelial factors by different size coronary arterial vessels has not been determined for vasopressin or serotonin, differential responses could account for some or all of the heterogeneity observed in this study.

Effect of autoregulation. The differential responses of the coronary microcirculation to serotonin and vasopressin may involve an autoregulatory change in segmental microvascular resistance to maintain total coronary resistance near control levels. In the case of serotonin, the arteriolar dilation may be at least in part an autoregulatory change in downstream vascular resistance to compensate for the upstream vasoconstriction after activation of 5-HT1 receptors in the large arteries. If perfusion pressure in arterioles less than 90 μm falls, the vessels may dilate to maintain coronary perfusion. Previous work by Chilian et al36 has shown that in the beating left ventricle of the cat under basal conditions, perfusion pressure in 100-μm arterioles is relatively low (approximately 50–55% of aortic pressure). With substantial upstream vasoconstriction and an increase in coronary flow, it is likely that pressure in 100-μm vessels will be substantially decreased. This could stimulate vasodilation of vessels less than 100 μm in diameter on an autoregulatory basis to maintain coronary flow.

A similar phenomenon may occur with vasopressin. Vasopressin may decrease resistance of large arteries and increase microvascular pressure with an autoregulatory adjustment to increase arteriolar resistance. This type of autoregulatory change to maintain constant flow during vasopressin has been described in the cerebral circulation.34 Such a mechanism may be involved in the coronary microvascular response to vasopressin.

Thus, autoregulatory adjustments stimulated by changes in microvascular pressure in the diameter of various sized coronary microvessels could account for some or all of the heterogeneity observed in our study.

Indirect actions of serotonin and vasopressin. Serotonin and vasopressin could have produced differential responses in the coronary microcirculation secondary to their effects on other humoral substances. Depending on the vascular bed, serotonin can stimulate α-receptors directly.37 In myocardium, for example, serotonin can be taken up into the sympathetic nerve terminal, causing an initial release of norepinephrine and subsequent inhibition of sympathetic neurotransmission.38,39 Previous studies in our laboratory indicate that the coronary microvasculature responds in a heterogeneous manner to neurally released or circulating norepinephrine after β-adrenergic blockade.40

Vasopressin also potentiates the effects of norepinephrine in rat mesentery38,41 and can act centrally to alter sympathetic outflow.21 In addition, vasopressin activates synthesis of prostaglandin E2.21 These indirect actions of serotonin and vasopressin could result in different vascular responses depending on the degree to which these secondary mechanisms are stimulated and the ability of a particular vessel size to respond to these stimuli.

Thus, four possible mechanisms may be involved in the differential response of the coronary circulation to serotonin and vasopressin. Each of these mechanisms or a combination of them may explain the observations in this study.

Summary

In conclusion, this study has demonstrated that coronary arteries and arterioles above and below the 90–100-μm level respond in a nonuniform manner, depending on the humoral stimulus. Serotonin constricts arteries and arterioles above 90 μm while simultaneously, arterioles below 90 μm dilate. Conversely, vasopressin minimally dilates arteries and arterioles above 90 μm while, simultaneously, arterioles less than 90 μm constrict. Further studies are needed to clarify the possible mechanism(s) involved in these differential responses.

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References

34. Segal SS, Duling BR: Communication between feed arteries and microvessels in hamster strated muscle: Segmental vascular responses are functionally coordinated. *Circ Res* 1986;59:283–290
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