Microvascular Blood Flow in the Normotensive and Spontaneously Hypertensive Rat

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SUMMARY To help assess the microcirculatory component in the etiology of hypertension, blood flow, vessel diameter, and the distribution of blood flow in the spontaneously hypertensive (SHR) and normotensive (WKY) microvasculature of the rat cremaster muscle have been determined in 7- to 8-week-old animals. By direct microscopic observation of the cremaster muscle, blood velocity (dual-slit method), arterial diameters (eyepiece micrometer), and blood flow calculated from these measurements were determined in each of five arterial branching orders from the entering artery (first order) to the terminal arteriole (fifth order). These measurements as well as the determination of the lengths between consecutive branches were made under control conditions and following the application of 1 mM adenosine to produce a dilated vasculature. Under control conditions, total cremaster blood flow in the SHR (11.1 ± 1.0 ml/min/100 g) was less than in the WKY group (21.1 ± 2.3); the distribution of total blood flow to each branching order was less in the SHR; and the arterial vessel diameters in the SHR group were smaller than the WKY counterparts except in the fifth order arteries. After dilation, blood flow increased in both groups, but flow in the SHR remained significantly less than in the WKY (27.0 ± 1.9 ml/min/100 g vs 45.5 ± 4.2). In spite of this, the control state flow differences beyond the second order vessels were eradicated by the dilation as were the diameter differences except in the first order vessel. Finally, under both control and dilated conditions, the distances between consecutive vessel orders were consistently longer in the SHR group suggesting a smaller number of branches. These results indicate that the higher vascular resistance and corresponding lower blood flow of the SHR can be attributed in part to: 1) smaller arterial diameters, locally and/or neurally controlled in the second through fifth order arteries and structurally determined in the first order artery; and 2) a smaller number of arterial branches. (Hypertension 4: 264–271, 1982)

KEY WORDS • essential hypertension • hypertension • microcirculation • blood flow distribution • microcirculation

THE spontaneously hypertensive rat (SHR) is frequently used as an animal model of human essential hypertension. The pathogenesis of the hypertension in the SHR is associated with an increasing total peripheral resistance (TPR) with minimal change in cardiac output,[1-3] although cardiac index has been found to increase.[4] Early studies by Folkow et al.[5-7] attributed this increased resistance to arterial wall hypertrophy with corresponding encroachment into the vessel lumen. Although these vessel wall changes were found to occur in the larger vessels, Furuyama[8] had already shown that wall hypertrophy in arteries less than 100 μm was not present. Since a considerable portion of vascular resistance resides in arterial vessels less than 100 μm in diameter there must exist other alterations contributing to the increased resistance. Factors thought to be involved include: 1) arteriolar rarefaction,[9-14] 2) augmented humoral responses,[11, 15-21] and 3) increased sympathetic nerve activity.[11, 18, 22, 23] A considerable number of recent findings support the vessel rarefaction hypothesis which states that the increase in TPR is due to a decreased number of small arterioles open to blood flow.[9] The link between the number of patent arterioles and TPR has been deduced from numerical counts which show a smaller number of vessels in the SHR. However, assessment of the hemodynamic effect of this rarefaction requires both blood pressure and flow information. The pioneering work of Bohlen et al.[24] has provided a characterization of the microvascular blood pressure profile in the SHR cremaster muscle, but the companion hemodynamic quantity, blood flow and its distribution, has been missing. Although Tobia et al.[2, 25] measured blood flow in SHR and WKY rats, his studies were confined to

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regional and whole organ circulations and provide no data on microvascular blood flow. Some microvascular velocity data in rat skeletal muscle are available (cremaster m.,[26] gracilis m.,[27] trapezius m.[28]) but there has been no systematic blood flow study of rat skeletal muscle in relation to branching orders. The main purpose of the present work is to provide basic information about blood flow and its distribution across the microvasculature of the cremaster muscle of SHR and WKY rats.

Methods

Eight male Wistar Kyoto (WKY) and eight spontaneously hypertensive rats (SHR) of the Okamoto and Aoki[29] strain, F-34 generation, were used in this study. All rats were 7 to 8 weeks old and weighed between 105 to 120 gs. Prior to preparing the cremaster muscle for microscopic observation each animal was initially anesthetized with a single dose of Nembutal (5.0 mg/100 g body weight i.p.), the minimum dose required to complete the surgery. The animal was then placed on a heated mat, a tracheal cannula inserted (3 cm length of PE-200 tubing), and the left carotid artery isolated from the surrounding muscle. Actual cannulation of the carotid artery, for systemic blood pressure recording, was left until after the cremaster muscle is prepared.

The technique used to prepare the cremaster muscle for microscopic study was adapted from the method reported by Baez.[30] Briefly, the cremaster muscle was separated from the scrotal sack by blunt dissection and kept moist by a constant flow Krebs solution maintained at 34°C throughout the surgical procedure. The Krebs solution consisted of NaCl 113 mM, dextrose 11.6 mM, KCL 4.7 mM, $MgSO_4 \cdot 7\ H_2O$ 1.2 mM, KH_2PO_4 1.2 mM, $CaCl_2 \cdot 2H_2O$ 2.6 mM, and $NaHCO_3$ 25 mM. The solution is bubbled with a gas mixture of 95% N_2 and 5% CO_2 to control the pH at 7.40. An incision was made on the caudal-ventral side of the muscle and continued to the level of the annulus inguinalis. Small bleeders were promptly tied off with 6-0 suture thread, which also served as tether points for spreading the tissue. The major vessels running within the mesoepididymus were cauterized and a cut made rostrally along the interface between the mesoepididymus and the cremaster muscle up to the annulus inguinalis. The testis was then introduced into the abdominal cavity. The muscle was spread over a specially designed optically clear heated pedestal which was thermostatically controlled to maintain the tissue at 34° ± 0.1°C, a value reported as the in situ temperature of the cremaster muscle.[28] The upper portion of the pedestal formed an open chamber which permitted the muscle to be superfused at a rate of 2 ml/min.

After completion of the muscle preparation, the left carotid artery was cannulated (18 cm length of PE-50 tubing) and connected to a BD two-way stopcock manifold to which an extra port was added to allow simultaneous blood pressure recording (Ailtech MS-20 semiconductor blood pressure gauge) and a constant infusion of a heparinized (10 units/ml) anesthetic solution (Inactin 0.076 mg/min). The infusion maintained the animal at a constant level of anesthesia, kept the blood pressure cannula patent at all times, and replaced lost fluid volume due to respiration, which occurred throughout the experiment. Following these procedures the animal, already secured to a mounting board, was placed on the stage of a Leitz Ortholux trinocular microscope with a 150 W xenon light source. The muscle preparation was allowed to stabilize for 1 hour before any measurements were made. After this stabilization period the criteria for rejecting the preparation for hemodynamic study were: 1) red blood cell extravasation (petechia) in the muscle tissue; 2) lack of vasodilatation (10% or greater) to a topically applied 10^{-3}M dose of adenosine; and 3) lack of vasoconstriction (20% or greater) to a topically applied 10^{-7}M dose of norepinephrine in the second order artery to be observed in the protocol.

Velocity measurements were made using a modified dual-slit method[31] and an on-line cross correlation technique.[32] The system dynamically analyzed the delay between upstream and downstream red blood cell photometric signals at a known distance apart to yield centerline velocity data. In our present study, the two signals were obtained by placing two phototransistors in the optical path of a projected vessel image within a specially constructed housing incorporating a head amplifier. The sensor spacing (referred to the preparation) was 5 μm with a 32× objective and 16 μm with a 10× objective. The signals were preamplified, bandwidth limited to 2 kHz and AC coupled before being fed into a commercial cross-correlation device (IPM). The velocity system was calibrated against a rotating wheel of known rate placed in the visual path of the microscope setup. The output of the cross-correlator was adjusted to provide a on-line display of the red cell velocity within the vessel under observation. The diameter of each vessel in which velocity was measured was determined with an eyepiece micrometer.

The arterial blood vessels of the cremaster muscle microvasculature were assigned to categories according to their branching order (see fig. 1). The major feeding artery (the cremasteric artery) was designated first order. Succeeding branches were assigned consecutive order numbers from 2 through 5; the 5th order vessels in this preparation directly supplied the capillaries.

Consecutive velocity and diameter measurements were made on 1st through 5th order arterial vessels. To allow efficient hemodynamic comparisons in the two groups of animals, these measurements were made at strategic sites within a standardized arterial pathway. This pathway permitted velocity and diameter measurements to be made on the first branch of each branching order as close as technically possible to the parent vessel. The only exception to this was in the 1st order vessel in which velocity was measured

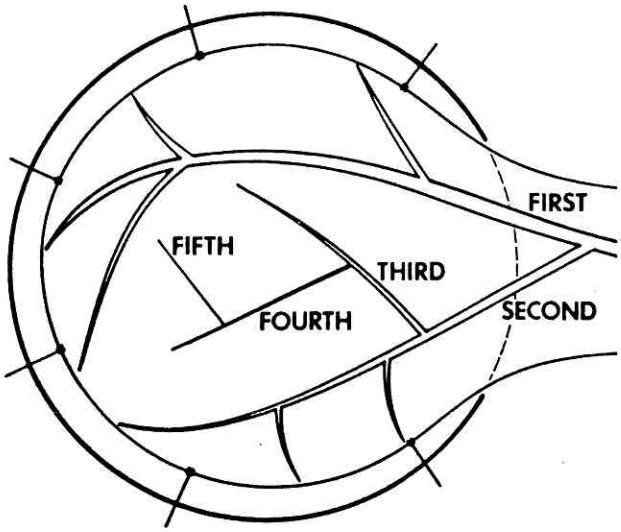

FIGURE 1. *Simplified cremaster muscle microvasculature pattern showing the nomenclature used to assign arterial vessels to the appropriate order (1st through 5th).*

slightly distal to the 2nd order branch, since the origin of the 1st order vessel was out of the field of view. A schematized pattern of figure 1 is shown in figure 2. In this figure, Q denotes the site at which velocity and diameter measurements were taken. In addition to these consecutive measurements in a single pathway, velocity and diameter were recorded in all remaining observable 2nd order vessels which arose from vessels outside the field of flow. Total cremaster flow was calculated as the sum of 1st order flow and the remainder of the 2nd order flows.

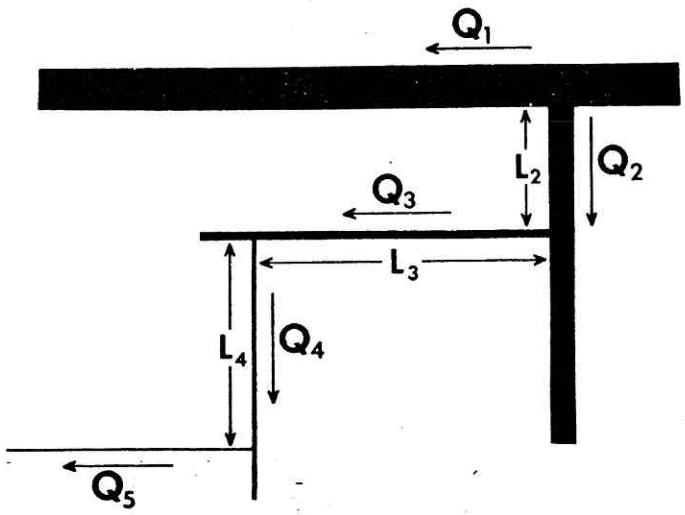

FIGURE 2. *Schematized pattern of figure 1. Q_i indicates the point at which arterial diameter and blood velocity recordings were made. L_i indicates intrajunctional vessel lengths.*

The mean blood velocity (V_m) together with vessel internal diameter (D) were used to calculate the blood flow (Q) from the formula $Q = V_m(\pi D^2/4)$. The measurements obtained from the cross-correlator were centerline velocity (V_{cr}), and a correction factor was needed to convert to mean velocity. For microvessels greater than 17 μm in diameter, the equation $V_m = V_{cr}/1.6$ was employed.[33] Below a vessel diameter of 17 μm the radial velocity profile changed and a different correction factor of 1.3 became more appropriate and was used.[34]

After control blood flow and diameter data were obtained, the muscle bed was dilated with a 1 mM topical dose of adenosine, which had no measurable effects on systemic blood pressure. Following this procedure, blood flow and diameter were again determined along the same arterial pathway.

In addition to flow measurements, the vessel segment lengths lying between corresponding branch points were recorded. These measurements are graphically illustrated in figure 2 by the double headed arrow labelled L_2 for intrajunctional distance of the 2nd order vessel and so forth. Additional vessel length measurements from other animals not included in the first part of the study were taken to increase the number of observations and reduce statistical variability.

The vascular input resistance of each arterial vessel order was calculated[33, 34] to permit assessment of the relative differences in input resistance as a function of branching order, animal group, and experimental conditions. These values for input resistance (R_i) were determined according to equation (1):

$$R_i = \frac{\Delta P_i}{Q_i} \qquad i = 1 \text{ to } 5, \qquad (1)$$

where ΔP_i = difference in pressure between the appropriate arterial order and the largest drainage vein; Q_i = blood flow in that particular artery; and i = branching order. Pressure values were computed by incorporating the percentages of systemic blood pressure for each arterial vessel order as taken from Bohlen et al.[24] and multiplied by the systemic blood pressure values measured in the present study.

Results

Arterial Diameter

In the control state, the SHR vessels were found to have smaller diameters than corresponding vessels of the WKY, at all but the 5th order artery level (table 1). The most prominent differences were seen in 1st and 3rd order vessels where the SHR arteries had 25% smaller average diameters than corresponding vessels in the WKY group. Administration of adenosine, a vasodilator, caused all vessels in both groups to increase in diameter but not to the same extent. Compared with the WKYs, all SHR vessels had a greater absolute and relative increase in diameter than corresponding vessels in the WKY group. These changes

TABLE 1. *Arterial Diameters in the Normotensive (WKY) and Spontaneously Hypertensive Rat (SHR) in the Control and Dilated States*

Vessel order	Control diameter* (μm)		Dilated diameter* (μm)		Diameter change† (%)	
	WKY	SHR	WKY	SHR	WKY	SHR
1st	83.0	61.8	93.6	81.1	14.0	37.0
SEM	3.6	3.3	2.3	2.6	3.8	4.6
p	0.001		0.003		0.006	
2nd	62.5	52.2	71.5	65.1	14.0	26.0
SEM	3.0	2.5	3.5	2.8	2.8	6.3
p	0.019		0.172		0.097	
3rd	36.2	26.7	44.5	41.1	25.0	56.0
SEM	2.6	1.6	2.9	2.5	8.1	12.1
p	0.008		0.375		0.050	
4th	13.7	11.9	19.3	20.4	48.0	73.0
SEM	0.5	0.7	3.2	2.1	13.9	15.9
p	0.050		0.956		0.265	
5th	7.3	6.7	9.6	11.2	49.0	66.5
SEM	0.2	0.2	1.3	0.6	8.0	8.7
p	0.097		0.349		0.153	

Normotensive rat blood pressure = 114.5 ± 2.9 mm Hg ($\bar{x}$ ± SEM); spontaneously hypertensive rat blood pressure = 145.5 ± 2.9 ($p < 0.01$).

p values determined by Student *t* test (*unpaired; †paired).

TABLE 2. *Blood Velocities in the Normotensive (WKY) and Spontaneously Hypertensive Rat (SHR) in the Control and Dilated States*

Vessel order	Control velocity* (mm/sec)		Dilated velocity* (mm/sec)		Velocity change† (%)	
	WKY	SHR	WKY	SHR	WKY	SHR
1st	35.4	42.6	65.7	56.4	93.0	36.5
SEM	3.0	5.2	3.4	4.7	17.0	7.1
p	0.246		0.129		0.008	
2nd	32.2	21.4	46.1	36.0	56.0	86.0
SEM	1.2	4.0	3.7	4.9	16.6	20.3
p	0.061		0.117		0.189	
3rd	15.5	12.3	18.9	18.1	23.5	52.0
SEM	1.2	2.1	1.5	3.1	6.3	15.7
p	0.202		0.805		0.115	
4th	10.4	5.9	11.4	10.4	37.6	93.0
SEM	2.0	0.8	1.4	1.3	25.0	28.0
p	0.054		0.606		0.161	
5th	3.7	3.0	6.0	6.1	132.0	175.0
SEM	0.6	0.4	1.0	5.0	87.0	78.7
p	0.322		0.922		0.717	

p values determined by Student *t* test (*unpaired; †paired).

eradicated control state diameter differences between the two groups *except* in the first order artery.

Blood Velocity

There proved to be no statistically significant difference in blood velocity between corresponding vessels in the SHR and WKY groups (table 2). The percentage by which the velocities changed following dilation also presented no obvious trends. The blood velocity of the WKY 1st order artery exhibited a significant increase over its SHR counterpart in the dilated state, but the end effect on blood flow proved to be marginal. The remainder of the data indicated no significant difference in the manner in which the blood velocity changed following dilatation.

Blood Flow

Under control conditions, total cremasteric blood flow in the SHR group was approximately one-half that of the WKY groups. When expressed in units of ml/min/100 g of tissue, the SHR value (mean ± SEM) was 11.1 ± 1.0 as compared to 21.1 ± 3.2 for the WKY group. Further, in all cases but the 5th order arteries, the SHR control blood flow was significantly less than the flow in the corresponding WKY vessels (table 3). After dilation by adenosine, total flow more than doubled in both groups. The SHR group still maintained a lower total flow but under these dilated conditions only the 1st and 2nd order arteries had significantly less flow than the WKY group. Calculated total blood flow for the SHR was 27.0 ± 1.9 ml/min/100 g tissue and 45.5 ± 4.2 ml/min/100 g tissue for the WKY. Thus, despite the presence of a highly efficacious vasodilator that tended to equalize the vessel diameters in the two groups, the SHR still maintained a lower total blood flow. In addition, the SHR group displayed a greater relative increase in blood flow following dilation than did the WKY group (table 3). This percentage increase in blood flow was progressively larger with increasing branching order.

Intrajunctional Vessel Lengths

Table 4 displays the intrajunctional vessel lengths for each group of animals. L_2 indicates the length of the second order vessel observed up to the point of the first branch, and so forth, for the L_3 and L_4 (see fig. 2). In each case, there is a significant difference in length of corresponding vessel segments, with SHR vessel lengths being longer by at least a factor of 2.

Calculated Values for Vascular Input Resistance

Values for vascular resistance were computed by incorporating the microvessel blood pressure data of Bohlen et al.[24] (table 5). At each vessel order the SHR group had a higher input resistance ranging between two to three times that of the WKY in the control state. Under dilated conditions, the relative differences between the two groups was reduced but still significant.

TABLE 3. *Calculated Arterial Blood Flow in the Normotensive (WKY) and Spontaneously Hypertensive Rat (SHR) in the Control and Dilated States*

Vessel order	Control flow* (nl/sec)		Dilated flow* (nl/sec)		Flow change† (%)	
	WKY	SHR	WKY	SHR	WKY	SHR
1st	300	170	641	413	128	148
SEM	41	16	44	31	18	13
p	0.009		0.011		0.386	
2nd	103	45	187	121	97	214
SEM	18	9	23	17	21	55
p	0.011		0.034		0.067	
3rd	15.8	6.9	30.4	25.0	106	322
SEM	2.5	1.8	4.1	4.3	23	71
p	0.010		0.380		0.011	
4th	1.45	0.66	5.56	3.43	113	485
SEM	0.24	0.12	2.47	0.93	29	15
p	0.012		0.429		0.040	
5th	0.165	0.103	0.577	0.678	197	721
SEM	0.031	0.013	0.106	0.094	51	193
p	0.090		0.483		0.027	

p values determined by Student *t* test (*unpaired; †paired).
First order flow is the sum of Q_1 and Q_2, as shown in figure 2.

TABLE 4. *Intrajunctional Arterial Vessel Lengths (L_i) in the Normotensive (WKY) and Spontaneously Hypertensive Rat (SHR)*

Vessel order	WKY (μm)	SHR (μm)	L_{SHR}/L_{WKY}
L_2	3260 ± 876 (7)	7380 ± 2130 (4)	2.26*
L_3	571 ± 94 (11)	1520 ± 395 (13)	2.67*
L_4	185 ± 330 (11)	380 ± 64 (13)	2.05*

Values are means ± SEM. (n) indicates number of animals per group.
*$p < 0.05$ level of significance (Student t test, unpaired).

Discussion

Flow-Resistance Relationship

A major goal of this study was to provide basic information about blood flow and its distribution across the cremaster microvasculature in the hypertensive and normotensive rats. The data show that when the control state blood flow distributions of the SHR and WKY groups are compared, the magnitude of SHR flow is demonstrated to be significantly less than that of the corresponding WKY branching orders except at the 5th order artery. The lower blood flow found in the SHR suggests that either the vascular resistance in the cremaster muscle is higher or, conversely, the perfusion pressure is less than in the WKY counterpart. The latter parameter, although not measured in this study, has been thoroughly examined by Bohlen et al.[24] whose findings indicate that the arteriovenous (AV) perfusion pressure is in fact greater in the SHR; consequently, the lower value for blood flow here is attributed to an elevated vascular bed resistance.

Bohlen et al.[24] have determined from extensive microvascular pressure measurements in the cremaster muscle of SHR and normal rats that there is no significant difference in the ratio of measured microvascular pressure to systemic pressure at corresponding branching orders; the ratios are 0.43 at the 1st order artery level and 0.11 at the 1st order venous level. Use of these ratios and the mean systemic pressure determined in our present work suggests that the mean SHR cremaster AV perfusion pressure is about 46.4 mm Hg and in the WKY about 36.8 mm Hg. Dividing these quantities by the corresponding measured total flows shows that in the control state the SHR vascular input resistance is 2.24 times greater than in the WKY. These vascular resistance differences are generally confirmed in whole body studies by Smith and Hutchins,[4] and in regional body studies by Tobia et al.[25] The findings of the latter authors have indicated that the SHR displays a total peripheral resistance approximately 1.8 times greater than the WKY counterpart but with an essentially unaltered regional blood flow. The difference between the unaltered blood flow found by Tobia et al.[25] and the results presented here which demonstrate a lower blood flow for the SHR suggest cremaster specific factors, unusual reactivity to the anesthetic used, or perhaps additional modifications present in the current 7- to 8-week-old SHR model, since the more recent animals tend to develop hypertension at an earlier age.[4, 9, 19, 24]

The adenosine-induced dilation of the cremaster microvasculature dramatically reduced the vascular resistance in both groups, but even under these conditions the SHR vascular resistance was about twice that of the WKY group. Obviously, simple vasodilatation was inadequate to equalize or significantly alter the ratio of SHR to WKY vascular bed resistance. These dilation studies have also brought about another important finding involving blood flow. The percentage by which the total flow increases following topical application of adenosine is similar among the SHR and WKY rats, being somewhat more doubled. The WKY group generally maintains this increase throughout the microvasculature, while the SHR group does not hold to the same trend. The increase in blood flow of the SHR rises dramatically in the higher vessel orders (smaller vessels), approaching an increase of over eightfold. We conclude that this disproportionate increase in flow in smaller vessels is due to a decreased number of 4th and 5th order arteries in the SHR which are available to handle additional blood flow.

TABLE 5. *Calculated Vascular Input Resistances (R_i) in the Normotensive (WKY) and Spontaneously Hypertensive Rat (SHR) in the Control and Dilated States*

Vessel order	Control			Dilated		
	WKY	SHR	R_{SHR}/R_{WKY}	WKY	SHR	R_{SHR}/R_{WKY}
1st	0.126	0.282	2.24	0.059	0.116	1.96
2nd	0.368	1.07	2.90	0.203	0.397	1.95
3rd	1.82	5.28	2.90	0.944	1.46	1.58
4th	15.9	44.1	2.77	4.14	8.48	2.05
5th	122.0	248.0	2.02	34.8	37.6	1.08

Resistance values listed in units of mm Hg · sec · $mm^{-3} \times 10^3$. Resistance computations incorporate microvessel blood pressure data from Bohlen et al.[24]

Anatomical and Morphological Microvascular Differences

Hutchins and Darnell[9] in 1974 associated the increase in vascular resistance of the SHR primarily with a decrease in the number of small arterioles. The intrajunctional vessel lengths found in our present study support this concept if this trend is present throughout the entire bed, since a decreased number of total branches may be consistent with the finding of longer lengths between the different branching orders of the SHR. The larger percent increase in blood flow following dilation is an additional reinforcement of the SHR rarefaction hypothesis. Folkow et al.[5-7] have postulated from SHR hindquarter studies that the increase in vascular resistance of this hypertensive model is due to a hypertrophy of the arterial wall and corresponding encroachment upon the vessel lumen. This condition has been shown to be present in large vessels[6, 21] (greater than 100 μm) but absent in microvessels[37] (less than 100 μm); thus indicates a decreased number of arterial vessels as the cause of the increased TPR. In conflict with other studies[9-13, 24, 37] we have consistently found the SHR to have a smaller resting diameter than the WKY for most of the arterial vessels examined. Based on the dilation studies, this difference in SHR diameter appears to have a morphological foundation only in the 1st order artery. The higher order vessels of the SHR dilate in the presence of adenosine to diameter values comparable to corresponding dilated WKY vessels, while the 1st order artery lacks this ability. These findings imply that under control conditions the smaller resting diameters of the 2nd through 5th order vessels of the SHR are due to nonmorphologically related factors such as increased sympathetic tone or enhanced endogenous catecholamine reactivity, while the 1st order artery is structurally unable to dilate as much as corresponding WKY vessels due to other physical factors.

It is important to note that in our studies we have made measurements in vessels along the same vascular patterns in each case, i.e., at a point just proximal to the 1st observable branch off the parent vessel and so forth through the higher orders of vessels (fig. 2). This scheme is not adhered to in other in vivo microvascular anatomical studies and could be the reason for the disagreement in arterial diameters. Indeed, a survey of the literature[9, 19, 24] quoting the 4th order SHR arteriole dimensions yields vessel diameters of 26, 12, and 8.7 μm. This disparity is present in the other vessels as well. Additionally the site at which the measurements were made in relation to the parent vessel is also of significance. It was not unusual to find arterial vessels that were larger in diameter at their distal end rather than at their origin. These findings, leading to an "inverse tapering" of the vessel, was especially evident among the larger arteries. The mean diameter of the SHR cremaster 1st order artery reported in this study was 61.8 μm for the control state. Other studies dealing with the same microvasculature[9, 11, 19, 24, 37] cite values considerably larger, ranging between 92.8 and 110.0 μm for comparably aged rats. But in our cremaster preparation, if one measured the 1st order artery at a point distal to its origin, the diameter would have more closely coincided with other published data.

In addition to these anatomical and morphological alterations possibly responsible for the lower blood flow and concomitant higher vascular resistance, recent publications indicate involvement of a multiplicity of other parameters. These factors include sympathetic innervation of normally noninnervated 4th order vessels in the SHR[23] and hyperviscosity of SHR blood due to polycythemia with an elevated hematocrit and red blood cell number.[38] Consequently, there appears to be no single factor responsible for the increase in vascular resistance, although the relative importance of each still remains to be established.

Thus, we conclude that the SHR has a lower total skeletal muscle blood flow than the WKY throughout its microvasculature due to a higher vascular resistance. This higher resistance results from: 1) smaller arterial diameters, which are morphologically determined in the largest artery and neurally or locally controlled in the smaller arteries; 2) a smaller number of arterial branches, which can be associated with longer intrajunctional lengths; and 3) other parameters not considered in this study, such as abnormal sympathetic innervation and blood hyperviscosity.

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