Distributions of Microvascular Pressure in Skeletal Muscle of One-Kidney, One Clip, Two-Kidney, One Clip, and Deoxycorticosterone-Salt Hypertensive Rats

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SUMMARY Studies were performed on the cremaster skeletal muscle in rats to investigate the microvascular changes that are associated with established one-kidney, one clip (1K1C) and two-kidney, one clip (2K1C) Goldblatt hypertension and with deoxycorticosterone (DOC)-salt hypertension. Rats were anesthetized with urethane and chloralose; and cremaster muscles with intact circulation and innervation were suspended in a controlled Krebs bath. Microvascular pressures and vessel diameters were measured at three consecutive arteriolar (A) and venular (V) branch levels. Arteriolar diameters (X ± SEM) in normotensive (NT) rats were 119 ± 7, 86 ± 5, and 31 ± 3 μm respectively for 1A, 2A, and 3A arterioles; and venule diameters were 218 ± 12, 141 ± 15, and 53 ± 7 μm respectively for 1V, 2V, and 3V venules. As compared to NT rats, there was a selective decrease in lumen size (percent reduction from control) for 1A and 2A (23% to 38%) in 1K1C and 2K1C rats and for 1A, 2A, and 3A (42% to 44%) in DOC rats. Venule diameters were not significantly different between normotensive and hypertensive animals at any branch level. Femoral artery pressures were significantly elevated (≥ 43%) in all three forms of hypertension; however, this increase in pressure was not proportionally transmitted throughout the microcirculation. This was evidenced by normal pressure in 3A arterioles and in all venules for 1K1C and 2K1C rats and by normal pressures in 3V and larger venules for DOC rats. Our findings indicate that elevated arterial pressure in chronic renal hypertension is not transmitted uniformly across all microvascular segments. Furthermore, our data indicate that there is a selective increase in resistance for larger cremasteric arterioles and that a substantial increase in resistance occurs in those arterioles (> 100 μm diameter) located proximal to the cremaster microcirculation. (Hypertension 6: 27-34, 1984)

KEY WORDS • microcirculation • renal hypertension • mineralocorticoid hypertension • intravascular pressures

THE microcirculation plays a dominant role in the control of peripheral resistance and is therefore a good location in which to study factors or phenomena that might alter total peripheral resistance. Arterial hypertension is one well-known cardiovascular phenomenon in which total peripheral resistance is elevated.1-2 Yet, little is known about the microvascular changes that contribute to the elevated peripheral resistance in hypertension. More detailed studies of the microvascular changes that accompany hypertension may provide valuable etiologic clues by focusing attention on those vascular sites that either produce or maintain the elevated peripheral resistance. In this regard, one goal of our study was to characterize the segmental arteriolar changes that are associated with three different models of experimental hypertension in the rat: one-kidney, one clip renal (1K1C), two-kidney, one clip renal (2K1C), and deoxycorticosterone (DOC)-salt hypertension.

Two vascular changes that could contribute to an elevated peripheral resistance are a decreased arteriolar radius3-4 and a decrease in the number of arterioles that are in parallel with each other.5-6 Studies of these vascular changes in the resistance vessels of the microcirculation have shown that these changes do not occur uniformly throughout the arteriolar tree.5-7 Thus, selective vascular changes at different microvascular levels could alter not only the magnitude but also the distribution of peripheral resistance in hypertension. With regard to this, an altered vascular resistance could affect not only the degree of pressure elevation but also the distribution of pressure across the microvascular bed.

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Methods

Production of Hypertension

Surgical procedures were used on Sprague-Dawley weanling rats at 3 weeks of age (weighing 50 to 70 g) to produce three experimental forms of hypertension. Prior to the surgical procedures, rats were anesthetized with a single intraperitoneal injection of pentobarbital (50 mg/kg). The 1K1C hypertension was produced by removing the left kidney and by placing a silver clip that had a 200 μm gap width on the right renal artery. For 2K1C hypertensive rats, both kidneys were left intact and a silver clip that had a 170 μm gap width was placed on the right renal artery. This gap size was selected to produce 2K1C rats that were age-, weight-, and pressure-matched with 1K1C rats. Acute microcirculation experiments were performed on 1K1C and 2K1C hypertensive rats (7 to 8 weeks old) approximately 4 weeks after these surgical procedures. To produce DOC-salt hypertensive rats, the left kidney was removed and a 30 mg pellet of deoxycorticosterone acetate was placed under the skin on the upper left flank. All rats that received deoxycorticosterone acetate were given drinking water supplemented with NaCl (1%) and KCl (0.3%) ad libitum. Two weeks after the initial deoxycorticosterone implant, these rats (5 weeks old) were lightly anesthetized with ether and were implanted with a 15 mg pellet of deoxycorticosterone acetate. DOC-salt hypertensive rats (7 to 8 weeks old) were used for acute microcirculation experiments approximately 2 weeks after implantation of the 15 mg pellet of deoxycorticosterone acetate.

Four weeks after the initial surgical procedures were used to induce hypertension, animals were lightly anesthetized with ether and the tail artery was cannulated to verify the presence of hypertension. Tail-cannulated rats were considered to be hypertensive if they exhibited and maintained a mean arterial pressure of 140 mm Hg or greater for at least 5 minutes. Before the acute microvascular experiments were performed, a minimum of 3 days was allowed to elapse after the tail-cannulation procedure.

Microcirculatory Preparation

For the acute microcirculation experiments, rats were anesthetized by intraperitoneal injection of urethane (800 mg/kg) and alpha-chloralose (60 mg/kg) and tracheostomized. Anesthetic supplements were given throughout each experiment when an animal demonstrated that it had entered a light plane of anesthesia that was defined by an active corneal reflex, whisker twitching, and a leg jerk in response to a toe pinch. Each anesthetic supplement consisted of 10% of the initial amounts of urethane and chloralose and was given by intraperitoneal injection with at least 30 minutes between individual supplements.

The cremaster skeletal muscle was prepared for microcirculatory observations with a technique previously described by Miller and Wiegman.9 With this procedure, the right cremaster muscle was isolated with intact circulatory and nerve connections to the rat. The animal was then positioned on a heating pad on a custom-designed plexiglass board so that the hindlegs of the rat straddled a raised, 45 ml, plexiglass tissue-bath chamber. Silk sutures were placed around the perimeter of the cremaster muscle and were fastened to the bath chamber wall to secure the cremaster over an optical port within the bath chamber.

A modified Krebs-bicarbonate solution was used to fill the tissue-bath chamber. The composition of the Krebs solution consisted of 25.5 mM NaHCO3, 112.9 mM NaCl, 4.7 mM KCl, 2.55 mM CaCl2, 2H2O, 1.19 mM KH2PO4, 1.19 mM MgSO4 7H2O, and 11.6 mM dextrose. This Krebs composition resulted in a measured osmolality (freezing point depression) of 280 to 290 mOsm. A combination of nitrogen and carbon dioxide were bubbled into the Krebs solution at flow rates which were adjusted to give a bath pH of 7.35 to 7.45, a bath pCO2 of 35 to 50 mm Hg, and a bath pO2 of 20 to 40 mm Hg. Bath temperature was maintained at 34.5° ± 0.5° C by an insulated heater coil in the bath chamber. These bath controls produced a consistent cremaster environment for microvascular observations.

After completion of the cremaster surgical procedure, the cremaster muscle bath was positioned on the stage of trinocular microscope for transillumination through the optical port in the bath chamber. Light from the cremaster was passed to a video camera, which provided an image of the cremaster microcirculation for storage on videotape and for display on a video monitor that had been calibrated with a ruled slide micrometer at magnifications from × 1000 to × 3200. Subsequent measurement of vessel lumen diameters were made during videotape playback and were accurate to ± 1.0 μm.
Rectal temperature of the rats was maintained between 35.5° and 38°C by the heating pad that was positioned beneath the rat. Mean arterial pressure was measured from the catheterized left femoral artery, and heart rate was obtained from skin electrodes that provided a Lead I electrocardiogram.

**Microvascular Pressure Measurement System**

Microvascular pressures in cremaster arterioles and venules were measured with a servo-null micropipette system (Instrumentation for Physiology and Medicine, San Diego, California). In our studies, the operational characteristics of this system were tested and found to be similar to those that have been reported for the servo-null technique by others. In our procedure, the polishing slurry contained 0.3 μm alumina particles that were suspended in 2M NaCl (20% solution by volume). A micro-manipulator was used to lower each pipette into a belt-driven, rotating dish that contained the polishing slurry. As each micropipette was beveled, the electrical resistance of the tip was continuously monitored and the pipettes were beveled until the micropipette resistance was reduced by approximately 10% of the initial value. This beveling procedure gave final micropipette tip diameters that ranged from 1 to 3 μm o.d. Prior to the microcirculation experiments, micropipettes were placed tip upward in a plexiglass pipette holder and were immersed in a reservoir of heparinized 2M NaCl for storage in a refrigerator.

**Experimental Protocol**

Three branch levels of arterioles (A) and venules (V) in the cremaster were selected for puncture in our study. The largest arteriole, which entered the cremaster through the cremaster stalk, was defined as the first-order arteriole (1A). Likewise, the large venule, which was paired with the 1A arteriole, was designated as the first-order venule (1V). Arterioles that branched from the 1A arteriole were defined as second-order arterioles (2A). Similarly, venules that branched from the 1V venule were called second-order venules (2V). Subsequent vessel branches from second-order arterioles or venules were termed, respectively, third-order arterioles (3A) or third-order venules (3V).

In our work, vessels were selected for micropuncture on the basis of their branching order. In addition, 1A and 2A arterioles were selected for micropuncture only if they were paired with 1V and 2V venules, respectively. Also, the selected 1V and 2V venules were always paired with arterioles. Selected 3A arterioles and 3V venules were not necessarily paired with one another; however, selected third-order vessels always terminated in finer branches that were connected with capillaries. We assumed that this vessel selection procedure provided a branching sequence for study that is representative of others in the network. Micropunctures were performed on 1A and 1V vessels as close as possible to the entry point of the cremaster stalk into the bath chamber. Micropunctures of the 2A and 2V vessels were performed within the midregion between the 1A or 1V branch point and the branch point of the selected 3A or 3V vessel. The 3A and 3V vessels were also punctured in the midregion for measurement of pressure.

In each acute experiment, a 3A arteriole was always punctured first for pressure measurements. After a completed measurement of 3A arteriolar pressure, the micropipette was moved upstream to the 2A arteriole from which the third-order branch had originated. A measurement of 2A arteriolar pressure was followed by measurement of 1A arteriolar pressure. This third-through first-order micropuncture sequence was designed to minimize any downstream effects of small platelet aggregates that could theoretically alter the distribution of pressure. Venular micropunctures were begun at the 1V branch level and were successively followed by micropunctures at the 2V and 3V branch levels. For an individual microcirculation experiment to be accepted in our study, it was necessary to have obtained successful pressure measurements from all three arteriolar and/or venular branch levels. Measurement of lumenal diameter for a given microvessel was made from images of the vessel that were videotaped during measurement of the microvascular pressure in that vessel.

Thus, the vessels and N sizes reported in Figures 1, 2, and 3 for vessel diameter are identical to those vessels in which pressure was measured in Figures 4, 5, and 6. The vessels for which diameters and pressures were reported were videotaped for minimum of 10 minutes during the measurement of microvascular pressure. On playback of the videotape, measurements of diameter were taken at 1-minute intervals, and the average for the 10-minute period was recorded as the vessel diameter. A 10-minute chart record of microvascular pressure, which corresponded to the same time period during which diameter was measured, was used to obtain pressure measurements at 1-minute intervals. The 10-minute average of these pressure measurements was then recorded as vessel pressure. If micropuncture of a microvessel resulted in a significant and persistent diameter change, the measurements were discarded. Group statistical comparisons were made using one-way analysis of variance and Student's t tests. Group differences were considered statistically significant at the p < 0.05 level.

**Results**

**Mean Arterial Pressure, Heart Rate, and Body Weight**

Four weeks after surgery to induce hypertension (rats 7–8 weeks of age), mean tail artery pressures of all hypertensive groups exceeded 140 mm Hg. How-
ever, under urethane and chloralose anesthesia, mean femoral artery pressures were approximately 19% lower than tail pressures under ether anesthesia for 2K1C renal and for DOC-salt hypertensive rats. In contrast, mean femoral artery pressures under urethane and chloralose were similar to mean tail artery pressures under ether in 1K1C hypertensive rats (Table 1). At the time of the acute microcirculation experiments, femoral artery pressure under urethane and chloralose anesthesia was significantly higher (≥43%) in hypertensive rats than femoral pressure in normotensive rats. Average heart rates under urethane and chloralose anesthesia in 1K1C and 2K1C renal hypertensive rats were similar to heart rates in normotensive rats. But, heart rates in DOC-salt hypertensive rats were significantly lower (19%) than heart rates in normotensive rats (Table 1).

For the acute microcirculation experiments, rats for all groups were selected to provide relatively the same age. At the time of the acute experiments, normotensive rats weighed from 140 to 203 g (X ± SEM = 185 ± 7 g), 1K1C renal hypertensive rats weighed from 158 to 247 g (X ± SEM = 205 ± 9 g), 2K1C renal hypertensive rats weighed 130 to 240 g (X ± SEM = 201 ± 10 g), and DOC-salt hypertensive rats weighed from 114 to 214 g (X ± SEM = 156 ± 12 g).

Microvascular Diameters

The lumen diameters of the 1A and 2A arterioles in normotensive animals, in which microvascular pressures were measured, were 119 ± 7.3 μm and 86 ± 5.4 μm, respectively. By comparison, the 1A arteriole (77 ± 4.9 μm) and 2A arteriole (53 ± 4.1 μm) in 1K1C renal hypertensive rats and the 1A arteriole (92 ± 9.4 μm) and 2A arteriole (58 ± 5.6 μm) in 2K1C renal hypertensive rats had significantly smaller lumen diameters (Figures 1 and 2). In contrast, diameters of 3A arterioles for the 1K1C (26 ± 2.7 μm) and 2K1C

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**TABLE 1. Comparison of Tail Artery Pressure under Ether Anesthesia with Femoral Artery Pressure and Heart Rate under Urethane-Chloralose Anesthesia**

<table>
<thead>
<tr>
<th>Animal group</th>
<th>Ether tail artery pressure (mm Hg)</th>
<th>Femoral artery pressure (mm Hg)</th>
<th>Heart rate (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT (8)</td>
<td>—</td>
<td>91 ± 4</td>
<td>403 ± 9</td>
</tr>
<tr>
<td>1K1C (8)</td>
<td>162 ± 5</td>
<td>164 ± 11†</td>
<td>425 ± 22</td>
</tr>
<tr>
<td>2K1C (6)</td>
<td>163 ± 6*</td>
<td>130 ± 8†</td>
<td>402 ± 16</td>
</tr>
<tr>
<td>DOC (6)</td>
<td>164 ± 12</td>
<td>134 ± 17†</td>
<td>337 ± 19†</td>
</tr>
</tbody>
</table>

NT, 1K1C, 2K1C, and DOC designate normotensive rats, one-kidney, one clip renal, two-kidney, one clip renal, and deoxycorticosterone-salt hypertensive rats, respectively. The number in parentheses indicates the number of animals in each group. Values are expressed as means ± SEM.

*Statistically significant difference at p ≤ 0.05 between tail pressure under ether and femoral pressure under urethane and chloralose.

†Statistically significant difference at p ≤ 0.05 between the normotensive group and each hypertensive.
(24 ± 2.6 μm) renal hypertensive rats were similar to 3A diameters (31 ± 3.1 μm) in normotensive rats (Figures 1 and 2). In DOC-salt hypertensive rats, arteriolar diameters were significantly reduced for the 1A (67 ± 6.7 μm), 2A (48 ± 5.9 μm), and 3A (18 ± 3.0 μm) arteriolar branch levels as compared to similar vessels in normotensive animals (Figure 3).

The 1V, 2V, and 3V in normotensive rats had diameters of 218 ± 6.9 μm, 141 ± 14.7 μm, and 53 ± 7.0 μm, respectively. In comparison, diameters of 1V, 2V, and 3V venules in 1K1C, 2K1C, and DOC-salt hypertensive rats were not statistically different from diameters of venules in normotensive rats (p ≤ 0.05) by either an F test or Student’s t test (Figures 1, 2, and 3). However, venules in each hypertensive group tended to have somewhat smaller mean diameters at all branch levels. This tendency was particularly apparent in 1V and 2V venules of DOC-salt hypertensive rats (178 ± 13.8 and 104 ± 9.3 μm, respectively).

Microvascular Pressures

The intravascular pressure (60 ± 5.1 mm Hg) for 1A arterioles in 1K1C renal hypertensive rats was significantly higher than pressure (46 ± 2.6 mm Hg) for 1A arterioles in normotensive animals (Figure 4). In addition, pressure was higher (50 ± 5.8 mm Hg) in the 2A arteriole of this hypertensive form as compared to pressure (43 ± 1.8 mm Hg) in the normotensive 2A arteriole. In contrast, pressures in 3A arterioles for 1K1C renal hypertensive rats (39 ± 3.3 mm Hg) were similar to 3A arteriolar pressures (37 ± 2.6 mm Hg) for normotensive rats. The 2K1C renal hypertensive rats had an elevated 1A arteriole pressure (53 ± 6.5 mm Hg), but pressures in 2A (41 ± 4.8 mm Hg) and 3A (34 ± 4.4 mm Hg) arterioles were similar to pressures in comparable vessels of normotensive rats (Figure 5). In contrast to normotensive rats, pressures in DOC-salt hypertensive rats were significantly elevated in 1A (62 ± 12.4 mm Hg), 2A (55 ± 4.8 mm Hg), and 3A (47 ± 3.1 mm Hg) arterioles (Figure 6).
Normotensive rats had 1V, 2V, and 3V venular pressures of 8 ± 0.9, 10 ± 0.5, and 11 ± 0.8 mm Hg, respectively. Similar pressures were found in the 1V, 2V, and 3V venules of 1K1C renal hypertensive rats, 2K1C renal hypertensive rats, and DOC-salt hypertensive rats (Figures 4, 5, and 6).

Discussion

The overall objective of our study was to test the hypothesis that the elevated total peripheral resistance in different forms of hypertension may involve selective microvascular changes. This hypothesis was tested by comparing the lumen diameters of and pressures in microvessels at several microvascular branch levels in the cremaster skeletal muscle of 1K1C renal, 2K1C renal, and DOC-salt hypertensive rats. Microvascular Diameters

In 1K1C and 2K1C renovascular hypertensive rats, the diameters of the 1A and 2A arterioles were significantly reduced (23% to 38%), whereas 3A arterioles were not different from comparable arterioles in normotensive rats (Figures 1 and 2). In DOC-salt hypertensive rats, there were substantial reductions (42% to 44%) in lumen diameters of 1A, 2A, and 3A arterioles (Figure 3). For venules of the renovascular and DOC-salt hypertensive rats, there were trends toward reduced lumen diameters, which were particularly striking for the 1V and 2V venules.

Several investigators have studied alterations in arterioles and venules with the development of several forms of hypertension. Wiegman et al.4 have reported that diameters of 1A arterioles are reduced and 1V venules are unchanged in the cremaster muscle of 1K1C rats. Click et al.16,17 studied small arterioles (30 to 50 μm) and venules (40 to 80 μm) in the cheek pouch of hamsters with the figure-8 form of renal hypertension and found no change in lumen diameters up to 70 days after induction of the hypertension. Joyner et al.18 found reduced diameters of larger arterioles (90 to 120 μm) in the cheek pouch microcirculation of hamsters 2 to 3 weeks after the induction of figure-8 hypertension, but the microvascular diameters of downstream arterioles were unaltered in this form of hypertension. Joyner et al.18 also reported significant reductions in diameters of venules at all venular levels in the cheek pouch.

In rats treated with DOC-salt, Friedman et al.19 showed vessel wall hypertrophy and reduced diameters for the superficial epigastric artery (127 μm) and for downstream arterioles (20–30 μm). Suzuki et al.20 also found reduced diameters in arterioles (< 40 μm) for the mesentery of rats that had been treated with DOC-salt. To our knowledge, there are no previous studies that have characterized the microcirculation in 2K1C renal hypertension. Collectively, the diameter data in our microvascular study and those of others indicate that reductions in arteriolar diameters are a common microvascular feature in renal and mineralocorticoid forms of hypertension. Some of the differences in the site and severity of the diameter reductions that have been observed by various investigators may be due to differences in species, in the tissue studied, and/or in experimental conditions for the various preparations. However in our study, comparisons of renal and mineralocorticoid hypertension were carried out under similar conditions. Thus, the differences in the site and severity of the diameter reductions that we observed are most likely related to a primary cause of the hypertension or to a secondary effect of the hypertensive process.

Microvascular Pressures

In our study, there was a significantly greater pressure drop between the femoral artery and the 1A arteriole for all hypertensive groups as compared to the pressure drop for normotensive rats. Femoral artery pressure was increased 80% in 1K1C rats, 43% in 2K1C rats, and 47% in DOC-salt hypertensive rats; but, 1A arteriolar pressures were only increased in each hypertensive group by 30%, 15%, and 35%, respectively. Thus, the increase in systemic arterial pressure was not proportionally transmitted to the 1A arteriole in the cremaster muscle. As further evidence for this point, the ratio for 1A arteriole pressure to femoral artery pressure was significantly decreased for all hypertensive groups (Figure 7). If resistance between the femoral artery and 1A arteriole had not changed during the development of hypertension, 1A arteriolar pressure would have increased in parallel with the femoral artery pressure. Our data strongly indicate that a significant component of increased peripheral resistance in hypertension occurs in vascular segments that are upstream of the 1A arteriole. Therefore, larger (> 100 μm) distributing arterioles also contribute significantly to increased peripheral resistance in sustained renovascular and DOC-salt hypertension in the rat.
measured pressures in arterioles (12–112 μm) and venules (16–127 μm) in the cheek pouch microcirculation of hamsters with figure-8 renovascular hypertension. They reported elevated pressures at all arteriolar levels, but found normal to low pressures in the venules. Normal venular pressures in the cheek pouch microcirculation were the result of an increased pressure drop across the microvascular segment, which included terminal arterioles, capillaries, and small postcapillary venules. Thus, an increase in resistance also occurred across this segment of the cheek pouch microcirculation in figure-8 hypertension.

In comparison to the renal and mineralocorticoid forms of hypertension, the cremaster muscle in the spontaneously hypertensive rat characteristically features a different kind of pressure distribution profile. Bohlen et al. found that pressures in spontaneously hypertensive rats were elevated in cremaster arterioles, capillaries, and venules in approximate proportion to the increase in systemic arterial pressure. Also, spontaneously hypertensive rats do not have reduced arteriolar diameters as compared to normotensive rats. In essence, Bohlen’s pressure data show that the ratio of microvascular pressure to systemic pressure in spontaneously hypertensive rats is essentially the same as the ratio for comparable vessels in normotensive rats. This suggests that an increased microvascular resistance is uniformly distributed across the cremaster microcirculation in spontaneously hypertensive rats.

By contrast, in the spinotrapezius muscle of spontaneously hypertensive rats, Zweifach et al. have reported that the elevated systemic pressure is reduced such that pressure is normal at the level of the capillaries and postcapillary venules. These investigators found that the largest reduction in pressure occurred at the level of the small precapillary arterioles (10–15 μm). The lack of agreement between the pressure distribution data for the cremaster and spinotrapezius may reflect regional vascular differences among skeletal muscles or methodological differences between these two laboratories.

In addition to a role for decreased arteriolar radius, a rarefaction of arterioles has also been proposed as a factor to account for increased peripheral resistance. Several studies have indicated that the number of small arterioles (10–30 μm) is reduced in skeletal muscle of spontaneously hypertensive rats and in the gracilis muscle of 1K1C hypertensive rats. Our pressure data for renovascular hypertensive rats do not suggest the presence of rarefaction at the small arteriolar level, which, if present, should have expressed itself as an increased pressure drop at that arteriolar site. However, in the DOC-salt hypertensive rats a rarefaction may be one factor contributing to the increased pressure drop that was observed between the small arterioles and small venules.

Concluding Remarks

In our study, reduced arteriolar diameters in the renal and mineralocorticoid hypertensive rats indicate

In the cremaster microcirculation of the 1K1C rats, pressure was significantly elevated in the 1A arteriole (30%) and appeared to be elevated in the 2A arteriole (16%); however, the 3A arteriolar pressure was clearly not different from that in the normotensive group (Figure 4). Similarly, in the microcirculation of 2K1C rats, there was a tendency toward an elevated (15%) 1A arteriolar pressure, but pressures in the 2A and 3A arterioles were clearly not different from pressures in comparable vessels of normotensive rats (Figure 5). In these two hypertensive groups, the increase in the pressure drop between the 1A and 2A arterioles indicated that there was an increased resistance across the 1A arteriole.

In comparison to the renovascular forms of hypertension, pressure was elevated at all three arteriolar branch levels in the cremaster microcirculation of DOC-salt hypertensive rats. Despite this elevation in arteriolar pressure, all venular pressures in DOC-salt rats were comparable to pressures in normotensive rats, which suggest that there was increased resistance and an increased pressure drop between the 3A arteriole and 3V venule (35%) in DOC-salt animals (Figure 6). Thus, these observations favor a site of increased resistance probably involving smaller precapillary arterioles.

There are only a few studies that have systematically measured the distribution of pressure across the microcirculation of hypertensive animals. Joyner et al. measured pressures in arterioles (12–112 μm) and venules (16–127 μm) in the cheek pouch microcirculation of hamsters with figure-8 renovascular hypertension. They reported elevated pressures at all arteriolar levels, but found normal to low pressures in the venules. Normal venular pressures in the cheek pouch microcirculation were the result of an increased pressure drop across the microvascular segment, which included terminal arterioles, capillaries, and small postcapillary venules. Thus, an increase in resistance also occurred across this segment of the cheek pouch microcirculation in figure-8 hypertension.

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Concluding Remarks

In our study, reduced arteriolar diameters in the renal and mineralocorticoid hypertensive rats indicate
a redistribution of microvascular resistance in skeletal muscle. It also seems reasonable to suspect that diameter reductions upstream of the 1A arteriole are responsible for the increase in resistance across this upstream vascular segment. Since observations in our study were confined to rats that were in the established or plateau phase of hypertension, there are two possible interpretations of our findings. First, the microvascular changes for the various forms of hypertension used in our study may be the result of unique etiologic processes characteristic of the various models of hypertension. There is evidence to indicate that renal and mineralocorticoid forms of hypertension may differ with respect to activation of the renin-angiotensin system, plasma volume factors, vasopressin, and sympathetic nervous system involvement. The relationship of these mechanisms to the observed microvascular changes require further systematic investigations and cannot be determined in the present study. A second possibility is that the observed diameter reductions may represent a microvascular process that is secondarily the result of hypertension and not the cause of hypertension. As such, the reduced arteriolar diameters in our study might be related to secondary changes in the structure of the vascular wall to counteract the increased systemic pressure. Accordingly, differences in the site and severity of the diameter changes may be a reflection of different rates of development of hypertension for the three models of hypertension used in our study. Different rates of development could easily be introduced by various experimental factors related to production of the various models of hypertension.

References

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