Morphometry of Canine Coronary Arteries, Arterioles, and Capillaries during Hypertension and Left Ventricular Hypertrophy


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SUMMARY. The mechanisms responsible for the increase in minimal coronary vascular resistance per unit mass of myocardium in animals with chronic hypertension and left ventricular hypertrophy remain unidentified. Because increases in wall thickness of resistance vessels in some vascular beds in response to hypertension may decrease luminal diameter, we hypothesized that similar changes may occur in the coronary vasculature. To test this hypothesis, we performed hemodynamic and morphometric studies on eight dogs with renovascular hypertension (one kidney, one clip) of 6 weeks' duration, and in six normotensive dogs. Hypertension evoked a 27% increase in left ventricular mass and was associated with a 67% increase in left ventricular minimal coronary vascular resistance per 100 g calculated from coronary perfusion measured with microspheres during adenosine infusion. The vasculature was fixed via perfusion of glutaraldehyde and tissue samples from the left ventricle were embedded in Epon. Wall:lumen ratios, determined by light microscopy, of coronary arteries and arterioles were similar in hypertensive and normotensive dogs. Lumen diameters of large epicardial arteries (>640 μm) of hypertensive dogs increased significantly so that wall:lumen ratios were normal despite an increased medial thickness. Ultrastructural analysis, however, showed an enhancement of the relative extracellular compartment of the tunica media of large coronary arteries of hypertensive dogs: 36.4 ± 3.4% vs. 26.5 ± 1.6% (mean ± SEM). Capillary numerical density and surface area (surface area:tissue volume) were significantly lower in the endomyocardium, while capillary volume density (volume:tissue volume) was lower in the midmyocardium and endomyocardium of hypertensive dogs compared to normotensives. We conclude that the luminal diameter throughout the coronary arterial tree is not reduced during early hypertension, and hence, vascular hypertrophy is not the anatomic basis for the increased minimal coronary vascular resistance in dogs with hypertension and left ventricular hypertrophy. (Circ Res 58: 38-46, 1986)

It is generally assumed that the walls of arteries and arterioles thicken in response to elevated arterial pressure and thereby contribute to the increased vascular resistance characteristic of the hypertensive state (Folkow et al., 1970, 1973; Weiss, 1974; Limas et al., 1980). However, this generalization is based primarily on data from large vessels such as the aorta (Wolinsky, 1972). The idea that vascular hypertrophy is not a condition necessary for the sustained hypertensive state (Freidman et al., 1971) is supported by data which show that the diameters of 1st through 4th order cremaster muscle arterioles at rest are similar in spontaneously hypertensive rats (SHR) and normotensive rats (Donovan and Longnecker, 1982). It has also been suggested that enhanced myogenicity, alterations in steady state tone, and cyclic vasodilation all contribute to hypertension (Greensmith and Duling, 1982).

Comparisons between arteries of various vascular beds suggest that a vessel's response to elevated arterial pressure differs with regard to the onset, type, and severity of the ultrastructural lesions (Greditzer and Fischer, 1978). Degenerative changes have been described in coronary arteries of hypertensive animals (Blackwinkel, 1970; Greditzer and Fischer 1978; Schmiebusch et al., 1980; Saer et al., 1981; Ogata et al., 1982) and patients with aortic coarctation (Vlodaver and Neufeld, 1968; Schneewiss et al., 1982). However, there have been no quantitative analyses of the response of the hierarchy of coronary vessels to hypertension.

Our objective was to compare, using morphometric techniques, the architecture of left ventricular coronary arteries, arterioles, and capillaries in normotensive dogs and dogs with hypertension and left ventricular hypertrophy in which hemodynamic and myocardial perfusion characteristics were also determined.

Methods

Induction of Renal Hypertension

Renal hypertension was produced in 14 adult mongrel dogs weighing 16–27 kg. The surgical procedures em-
played to evoke hypertension and left ventricular hypertrophy, previously described in detail (Mueller et al., 1978), are briefly summarized. The dogs were anesthetized with sodium pentobarbital (30 mg/kg, iv), mechanically ventilated with room air, and the abdomen was entered through a midline incision. A clamp, described by Ferrario et al. (1971), was placed around the left renal artery and tightened until a thrill could be felt distal to the clamp (Koyanagi et al., 1982). After a right nephrectomy, the incision was closed and the dog was returned to the kennel.

Five weeks after the induction of hypertension, the eight surviving dogs and six control, normotensive dogs were anesthetized with pentobarbital (30 mg/kg, iv), placed on the respirator, and a left thoracotomy was performed via the 4th intercostal space. Cannulas were placed in the descending aorta and in the left atrium through its appendage, tunneled subcutaneously, and exteriorized dorsally.

**Experimental Protocol**

After a 1-week period of recovery, the dogs were returned to the laboratory, placed in a harness, and hemodynamic and myocardial perfusion measurements were obtained in the awake state. Approximately one-half hour prior to these measurements, the dogs were sedated with 6–15 mg morphine (iv). Atrio and left atrial pressure were obtained with Statham p23AA and p238B transducers, respectively. The electrocardiogram and pressure data were monitored continuously and recorded on a direct-writing oscillographic recorder. When hemodynamic parameters were stable, baseline (control) myocardial perfusion was measured by injecting microspheres into the left atrium. Five minutes later, adenosine (4.7 μg/kg per min, iv) was infused. This dose has been shown to produce maximal vasodilation in dogs (Mueller et al., 1976). Once heart rate and blood pressure stabilized, usually within the 1st minute of infusion, a second measurement of myocardial perfusion was obtained with microspheres. The adenosine infusion was continued for 4 minutes after the microspheres were injected.

After these measurements had been completed, the dogs were anesthetized with pentobarbital (30 mg/kg, iv), and the coronary vasculature was fixed via vascular perfusion, as described in a subsequent section.

**Measurement of Regional Myocardial Perfusion**

Carbonized radioactive microspheres (6.3 ± 0.3 × 10^6), 15 μm in diameter and labeled with 85Sr or 90Nb, were injected through the left atrial cannula which was subsequently flushed with 10 ml of saline. Before injection, the microsphere vials were agitated with a mechanical mixer for at least 3 minutes. The microspheres were suspended in a solution containing 10% dextran and 0.05% Tween 80. Beginning 20 seconds before injection and continuing 90 seconds after flushing the atrial cannula, an arterial reference sample was withdrawn from the aortic cannula at a constant rate of 2.06 ml/min. During this period, the electrocardiogram showed no arrhythmias or significant changes in heart rate. Arterial pressures were similar before and after microsphere injection.

For analysis of regional myocardial perfusion, tissue samples weighing approximately 10 g were excised from the mid-section of the left ventricular wall. Each transmural sample was divided into subendocardial, midwall, and subepicardial layers of equal thickness, weighed, placed in a plastic counting vial, and counted for 5 minutes in a 3-inch well detector. We calculated myocardial perfusion, (MP, ml/min × 100 g) from the formula:

\[ MP = \frac{C_m \times 100 \times RBF}{C_r} \]

where \( C_m \) = counts/g of myocardium, RBF (reference blood flow) = reference artery withdrawal rate, and \( C_r \) = total counts in the reference blood samples.

**Preparation of Tissue for Microscopy**

After hemodynamics and myocardial perfusion were measured, the dogs were anesthetized with sodium pentobarbital (30 mg/kg, iv) and a thoracotomy via the 3rd intercostal space was performed. Two cannulas were positioned in the ascending aorta via the brachiocephalic and left common carotid arteries. One cannula was attached to a pressure transducer, while the other was on line with the tubing passing through a peristaltic pump. The cannulas were tied into position and the aorta was clamped between the left common carotid and subclavian arteries. After heparinization, the heart was arrested by injecting 10 ml of procaine into the left ventricle, and the right atrium was opened to create an outflow channel. Without interruption, 1 liter of Lockes solution followed by 2 liters of glutaraldehyde fixative solution (1.5% glutaraldehyde, 0.1 M cacodylate, 0.2% paraformaldehyde, 0.01 M CaCl2, pH 7.4) were perfused through the coronary circulation (Tomanek and Karlsson, 1973). Aortic pressure was continuously monitored, and the flow of the perfusate was adjusted to maintain a pressure in the 100-120 mm Hg range.

All of the hearts used in this study remained arrested in diastole and showed evidence of uniform fixation. After determination of heart and ventricular weights, the hearts were placed in the fixative solution overnight. The left ventricle then was dissected to obtain multiple tissue samples. From each left ventricle, we excised: (1) the left anterior descending artery (LAD) and its first two branches, (2) the terminal branches of the LAD at the apex of the heart, (3) four epicardial regions, (4) two midmyocardial layers, (5) the two papillary muscles, (6) two endomyocardial regions, and (7) three small branches of the circumflex. For each sample site, except those involving the LAD and its branches, two specimens were processed and embedded in Epon. One-micron-thick sections were prepared on an ultratome, placed on glass slides, and stained with Richardson’s solution.

**Morphometrics**

We projected images of these sections onto paper and outlined (1) the luminal diameter (the least diameter was used in order to avoid the effects of obliquely sectioned vessels), and (2) the vessel’s wall at the points where the diameter was determined. Wall thickness is defined as the distance from the lumen to the outer edge of the media. For most vessels, these procedures were carried out at 1440X. In the case of larger vessels, the diameter was outlined at lower magnifications, but wall thickness was demarcated at 1440X. Subsequently, diameters were measured directly from the tracings, the values corrected for magnification, and the vascular wall:lumen ratios and corresponding lumen diameter were analyzed by computer. For each vessel, wall thickness was measured at opposite ends of a line representing the lumen diameter, and the two wall thickness values were averaged. Lumen
diameters (>15 μm) were measured to the nearest 0.5 mm with a rule, while smaller diameters (<15 μm) and all wall thickness measurements were obtained with an ocular micrometer and were measured to the nearest 0.1 mm. Capillary cross-sectional profiles were traced from epicardial, midmyocardial, endomyocardial, and papillary muscle specimens at 1440×. To minimize the inclusion of venules, we included only those profiles with diameters <10 μm. For each sample, we traced approximately 600–700 capillaries from our fields. The tracings were analyzed with a Quantimet Image Analysis Instrument to determine capillary numerical density; capillary surface area, or surface density, and capillary luminal volume:tissue volume, or luminal volume density. Details concerning this method have been published previously (Crisman and Tomanek, 1985). To assess the magnitude of myocardial hypertrophy across the ventricular wall, we traced the outlines of approximately 35 cell profiles cut perpendicular to the long axis of the cell at the level of the nucleus, and measured their cross-sectional areas with a digitizer (Tomanek et al., 1979). Arteries and arterioles were subsequently located under a light microscope, and tissue blocks were trimmed to isolate a particular vessel. Thin sections were prepared with a diamond knife and stained with uranyl acetate and lead citrate. The vessels then were photographed with an electron microscope. In selected large epicardial arteries, we determined the relative volume fractions of the media occupied by myocytes and extracellular components with a digitizer interfaced to a programmable calculator.

**Statistics**

Statistical comparisons are based on Student’s t-test (one-tailed) with a P ≤ 0.05 selected to denote significance. Data are presented as a mean ± SEM.

**Results**

**LV Mass, Hemodynamics, and Myocardial Perfusion**

Six weeks after undergoing the surgical intervention to induce renal hypertension, the experimental dogs exhibited a 54% increase in mean arterial pressure and a 27% increase in left ventricular weight:body weight ratio (LVW:BW), compared to their normotensive controls (Fig. 1; Table 1). The

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**TABLE 1**

Hemodynamics in Control and Hypertensive Dogs at Rest and during Maximal Coronary Vasodilation (MCV)

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Hypertensive group</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>MCV</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>106 ± 12</td>
<td>124 ± 14</td>
</tr>
<tr>
<td>Mean aortic pressure (mm Hg)</td>
<td>85 ± 3</td>
<td>52 ± 5*</td>
</tr>
<tr>
<td>Myocardial perfusion (ml/min × 100 g)</td>
<td>95 ± 14</td>
<td>372 ± 59*</td>
</tr>
<tr>
<td>Endo:epi ratio</td>
<td>1.28 ± 0.07</td>
<td>0.80 ± 0.06*</td>
</tr>
<tr>
<td>Coronary resistance (mm Hg/ml × min × 100 g)</td>
<td>1.01 ± 0.17</td>
<td>0.15 ± 0.02*</td>
</tr>
<tr>
<td>Total coronary resistance (mm Hg/ml × 100 g × min)</td>
<td>0.16 ± 0.02</td>
<td>0.21 ± 0.04</td>
</tr>
</tbody>
</table>

Values are means ± SEM. Statistically significant differences (P ≤ 0.05) are noted as follows: *Rest vs. MCV (paired t-test) and †control group vs. hypertensive group (unpaired t-test).
surgical procedure evoked hypertension and LVH in all experimental dogs. These changes were accompanied by a 67% increase in left ventricular minimal coronary vascular resistance (LV MCVR) per 100 g as calculated by left ventricular perfusion and mean arterial pressure during maximal vasodilation with adenosine. Although total LV MCVR tended to be higher in the hypertensive than in the normotensive dogs, the difference between the mean values did not attain statistical significance (Fig. 2).

Arterial and Arteriolar Morphometry

Figure 3 illustrates vascular wall thickness:lumen diameter ratios for various size arteries and arterioles comprising the left ventricle. From this histogram, it is evident that wall:lumen ratios for any given class of lumen diameters are quite similar for the experimental and control dogs. These data suggest that hypertension and LVH were not accompanied by a reduced luminal diameter due to increased wall thickness.

We considered the possibility that hypertension may have increased both wall thickness and lumen diameters, leaving their ratios unchanged. In general, this does not appear to have occurred, since the percentage distribution of vessel diameters is approximately the same for the two groups (Fig. 3). We selectively analyzed two homogeneous groups of vessels. The first group consisted of epicardial arteries >640 \( \mu \text{m} \) which included the proximal 2 cm of the left anterior descending artery and its first two branches (1 cm or less from their points of origin). A second group consisted of intramural arterioles (with luminal diameters ranging between 7 and 75 \( \mu \text{m} \)) obtained from the middle layer of the ventricular free wall. These two groups of vessels provided homogeneity with regard to size, type, and location. As seen in Table 2, the mean diameter of the large epicardial arteries is significantly larger in the hypertensive than in the normotensive dogs. Although wall thickness also tends to be greater, the difference does not attain statistical significance. The same is true for the wall:lumen ratio. Thus, it would appear that the increase in luminal diameter of large epicardial arteries associated with hypertension offsets the tendency for greater wall thickness. In contrast, the dimensions of intramural arterioles were found to be nearly identical in hypertensive and normotensive dogs (Table 2).

Using electron microscopy, we evaluated the morphological characteristics of arteries and arterioles from the same tissue blocks used for light microscopy. The morphology of arterioles (<100 \( \mu \text{m} \) lumen diameter) was similar in the two groups of dogs. We did not discern any consistent differences between hypertensive and normotensive groups in small arteries <400 \( \mu \text{m} \), although animal-to-animal variation was evident, e.g., thickness of the subendocardial space, shape of myocytes, and thickness of the internal elastic membrane. In contrast, an increased extracellular area with collagen accumulation in the tunica media was observed in the larger (>640 \( \mu \text{m} \)) epicardial arteries of hypertensive dogs. Therefore measured the volume percent of myocytes and the extracellular compartment in the first branches of the left anterior descending coronary artery. These data, obtained from electron micrographs with a digitizer, are illustrated in Figure 4. The relative volume (volume density) of the extracellular compartment was 37% greater in hypertensive than in normotensive dogs. This relative increase was associated primarily with an enhancement of collagen (Fig. 5). Myocytes in these large vessels from hypertensive dogs were not more irregular in shape than those from control dogs.

Capillary Morphometry and Myocardial Cell Hypertrophy

Hypertension-induced hypertrophy was associated with a relative reduction in the capillary bed (Fig. 6). Capillary density tended to be lower in the experimental dogs in all four left ventricular myocardial layers sampled—epimyocardial, midmyocardial, endomyocardial, and papillary muscle. However, only the difference for the endomyocardial layer attained statistical significance. Mean capillary diameter was not affected by hypertension and hypertrophy. Capillary surface area:tissue volume was lower in endomyocardial samples of hypertensive dogs, whereas capillary luminal volume:tissue volume was significantly lower in the midmyocardium and endomyocardium of hypertensive dogs.
The decrements in capillarity are related to the magnitude of myocardial hypertrophy in a given region of the ventricular wall. Figure 7 illustrates the mean myocyte cross-sectional area of midmyocardium, endomyocardium, and papillary muscle expressed as a percent of the epimyocardial mean. Ratios have been used because of the variation in body and heart size of the dogs used in this study. In control dogs, myocyte cross-sectional area in the midmyocardium is similar to that in the epimyocardium, whereas, in the endomyocardium, the cells are slightly (8%) larger. However, in dogs with LVH, cell sizes in the midmyocardium and endomyocardium are 26% and 41% greater than in the epimyocardium. These findings indicate that cell size showed a gradient across the ventricular wall during LVH associated with hypertension.

Discussion

This study is the first to assess quantitatively the response of the hierarchy of the coronary vasculature to chronic hypertension associated with LVH. Our major finding is that wall:lumen ratios of arterioles and arteries are not increased during a 6-week period of hypertension, and therefore do not contribute to the elevated MCVR/100 g. An increase in medial thickness of the large epicardial arteries characterized by an enhanced extracellular compartment in hypertensive dogs was accompanied by an increase in luminal diameter. Thus, these extensive quantitative data fail to implicate increases in wall:lumen ratio as a structural basis for the decrement in coronary reserve characteristic of LVH.

Wall:Lumen Ratio and Vascular Growth

That coronary arteries undergo ultrastructural alterations during experimentally induced hypertension has been shown by descriptive studies. Intimal changes including fibrin formation (Huttner et al., 1968; Bhan et al., 1978) and endothelial cell organ-
nelle proliferation (Saer et al., 1981) have been reported in experimental hypertension. Medial smooth muscle hypertrophy has been described in large coronary arteries of deoxycorticosterone acetate (DOCA) hypertensive rats (Greditzer and Fischer, 1978). Such an adaptation has also been noted in the small coronary arteries and arterioles in young patients with aortic coarctation (Schneckwiss et al., 1982). However, medial hypertrophy does not necessarily cause a reduction in luminal diameter. Another study on patients with aortic coarctation demonstrated that, despite an increase in the cross-sectional area of the left and right coronary arteries, luminal cross-sectional area increased rather than decreased (Vladovar and Neufeld, 1968), a finding that is consistent with our own data. That long-term hypertension may result in reduced \( \text{wall:lumen ratios in myocardial arterioles} \) has been documented recently in 7-month-old SHR (Tomanek et al., 1985).

Our study suggests that hypertension, at least in the early stage, does not lead to a reduction in luminal diameter. In the case of the large epicardial arteries (>640 \( \mu m \)), luminal diameter increased, a factor which offset any medial hypertrophy. The only other relative homogeneous population of vessels that we were able to analyze separately was the intramural arterioles from the midmyocardium. In this population, we found no difference in either lumen diameter or wall:lumen ratio. Therefore, it is unlikely that medial hypertrophy caused a decrease in luminal diameter of any size of artery or arteriole. Considering that—with the exception of the largest epicardial arteries—the number of vessels of a particular size was determined by chance, it is important to note that the ratio between the numbers of vessels from normotensive and hypertensive dogs is fairly constant throughout the hierarchy of lumen sizes. Therefore, there is no evidence to indicate that shifts from one size class to another occurred in the hypertensive dogs.

Since LV MCVR per unit mass but not total LV MCVR increased significantly in hypertensive dogs, it would appear that the former was primarily a...
consequence of the increased LV mass. It is evident from the capillary data that these vessels do not grow in proportion to the magnitude of hypertension-induced LVH, a finding that is consistent with numerous studies (Roberts and Weam, 1941; Ljungqvist and Unge, 1973; Lund and Tomanek, 1978; Anversa et al., 1979; Tomanek et al., 1982). Whereas capillaries do not contribute substantially to resistance, the reduction in capillary volume noted in this study could limit oxygen availability to the myocardial cell during conditions requiring prolonged enhanced ventricular work. Moreover, it is reasonable to predict that if capillary growth lags behind the increase in muscle mass, arteriolar growth would also lag. Under these conditions, as shown by our data, LV MCVR/100g would be expected to increase.

However, the increase in LV MCVR/100g was considerably greater (67%) than the increase in LV weight:body weight ratio (27%). If inadequate growth of the vascular bed were the only contributor to the increased LV MCVR, one would expect this increase to be proportional to the magnitude of the hypertrophy. Therefore, some decrease in the total cross-sectional area of the coronary bed may have occurred as a consequence of hypertension. This possibility is supported by the trend toward higher total MCVR values in the hypertensive dogs. Total MCVR is a measure of the total cross-sectional area of the coronary bed. Subsequent discussion will address three factors which may have contributed to the increased MCVR: (1) decreased capacity for maximal vasodilation, (2) extravascular compression, and (3) vascular rarefaction.

Capacity for Maximal Vasodilation

It is possible that lumen diameter of arteries and/or arterioles in the hypertensive dogs was less in the in vivo, vasodilated state than after diastolic arrest and vascular perfusion. There are two potentially important differences between these conditions.
First, although higher adenosine doses than those employed in these experiments will not produce further vasoconstriction, we cannot eliminate the possibility that in vivo vascular reactivity to the vasoconstrictor differs in hypertensive and normotensive dogs. Second, since we fixed the coronary vasculature in diastole—arrested, nonworking hearts, we were not able to assess the contribution of possible decreases in myocardial compliance (i.e., an increase in diastolic stiffness) in hypertensive dogs with LVH. In either circumstance, one cannot exclude the possibility that in vivo dimensions of the coronary resistance vessels were less in hypertensive than normotensive dogs. However, our data do demonstrate that anatomical, as distinguished from functional, wall:lumen ratio is not reduced in the coronary arteries and arterioles during the first 6 weeks of hypertension and LVH.

Our results do not provide any support for the concept that MCVR was affected by the increased extracellular compartment of the tunica media, which is composed primarily of collagen. First, the increase in collagen was limited primarily to the large epicardial vessels which contribute little resistance. Second, the luminal diameters of these arteries were slightly larger, rather than smaller, in hypertensive compared to normotensive dogs. Elevated collagen synthesis and deposition in larger arteries of spontaneously hypertensive and DOCA-hypertensive rats have been reported (Ooshima et al., 1974; Spector et al., 1978) and were suggested to be one of the sequelae of hypertension. In the aorta, enhancement of medial collagen occurs only after long-term (10-month) hypertension in rats (Wolinsky, 1972; Schmiebusch et al., 1980). However, the accumulation of medial collagen after only 6 weeks of hypertension is consistent with a recent study which demonstrates a similar change in the left coronary artery of spontaneously hypertensive 45-day-old rats (Anversa et al., 1984). That collagen could play a role in vascular distensibility is supported by the finding that arterial blood pressure decreased when DOCA-hypertensive rats were administered β-aminopropionitrile, an agent which interferes with the formation of cross-linked collagen (Iwatsuki et al., 1977). In hypertensive states where collagen enhancement may occur in resistance vessels, as described in humans with aortic coarctation (Schneeweiß et al., 1982), vascular distensibility could be compromised and MCVR elevated.

Extravascular Compression

Extravascular compression is a factor which limits flow in the myocardium and thereby elevates resistance. In our experiments, compressive forces were higher in hypertensive than in normotensive dogs during adenosine infusion. This factor could have contributed to the increased MCVR in the hypertensive dogs. A recent study (Harrison et al., 1985) indicates that when differences in extravascular compression are nearly totally eliminated—by employing a blood-perfused, contracting, vented ventricle—the differences between the two groups are no longer apparent. However, Mueller et al. (1978) and Scheel et al. (1984) did demonstrate that MCVR was increased even when differences in extravascular compression were minimized in normotensive and hypertensive animals. Thus, the contribution of extravascular forces to MCVR in hypertensive dogs is controversial at this time.

Vascular Rarefaction

An absolute decrease in the number of arterioles in the hypertensive dogs would lead to an increased MCVR. Such a rarefaction generally is due to a decrement in the number of the smallest resistance vessels (Mulvany, 1983).

Studies on spontaneously hypertensive rats suggest that the number of arterioles is less than in normotensive Wistar-Kyoto rats in the mesentery (Henrich et al., 1978) and cremaster muscle (Hutchinson and Darnell, 1974). Whereas no data are available regarding arteriolar rarefaction in the myocardium during hypertensive states, one can appreciate that even a small reduction in the number of these principal resistance vessels would have an appreciable effect on MCVR. Arteriolar numerical density is difficult to assess in the myocardium because these vessels are sparse. However, future studies should address this potential contributor to decreased coronary reserve.

In conclusion, our data indicate that myocardial hypertrophy is the major contributor to the increased MCVR per unit mass during early hypertension. Although we find no evidence for a decreased luminal diameter due to increased medial thickness in coronary arteries and arterioles of various sizes, we cannot rule out the possibility that either increased extravascular forces or rarefaction of vessels due to hypertension contributes to enhanced MCVR. We therefore support the view that the sustained hypertensive state is not necessarily dependent upon vascular hypertrophy (Freidman et al., 1971). However, we recognize that decreases in luminal diameters of coronary arterioles and arteries as a consequence of medial hypertrophy could develop with long-term hypertension.

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