Prevention of Coronary Vasodilator Reserve Decrement in Spontaneously Hypertensive Rats

ROBERT J. TOMANEK, ROGER D. WANGLER, AND CAROL A. BAUER

SUMMARY Spontaneously hypertensive rats (SHR) demonstrate an elevated minimal coronary vascular resistance by the seventh month of age. In an attempt to determine the role of long-standing hypertension in the etiological process of the elevated minimal coronary vascular resistance, we treated SHR and normotensive Wistar-Kyoto rats (WKY) with the vasodilator hydralazine from the time of weaning (1 month) until they were 7 to 8 months of age. The animals were instrumented 24 hours after their last drug dose and then studied on the following day. Using microspheres we measured myocardial perfusion in conscious rats at rest and during maximal coronary dilation induced with dipyridamole infusion. Hydralazine maintained arterial blood pressures in the normotensive range throughout the experimental period, but had little effect on left ventricular weight/body weight ratios (control SHR = 2.95 ± 0.07, treated SHR = 2.73 ± 0.08, control WKY = 2.39 ± 0.09, mean ± SEM). In treated SHR, left ventricular minimal coronary vascular resistance (per 100 g of tissue) was markedly lower (0.10 ± 0.01) than in the controls (0.16 ± 0.01) and not significantly different from that of WKY (0.11 ± 0.01). Similar differences were noted in the nonhypertrophic right ventricle (treated SHR = 0.08 ± 0.01, control SHR = 0.16 ± 0.01, control WKY = 0.10 ± 0.01). Total minimal coronary vascular resistance was also lower in both ventricles of the treated SHR compared with their nontreated controls. In WKY, hydralazine treatment significantly reduced blood pressure and total minimal coronary vascular resistance (p < 0.01). Histological assessment of resistance vessels (luminal diameter < 200 μm) suggests that the wall/lumen ratio was greater in SHR than in WKY and that hydralazine treatment tended to decrease the ratio in SHR but not in WKY. These data suggest that the increased minimal coronary vascular resistance in SHR is due to long-standing hypertension rather than to genetic variations or to the presence of myocardial hypertrophy. The data from WKY also support the contention that minimal coronary vascular resistance can be modified by chronically attenuating arterial blood pressure. (Hypertension 7: 533-540, 1985)

KEY WORDS • minimal coronary vascular resistance • myocardial perfusion • coronary reserve • hydralazine • cardiac hypertrophy

LEFT ventricular hypertrophy (LVH) due to hypertension has been associated with deficits in coronary circulation in experimental animals and humans. Coronary vasodilator reserve has been shown to be decreased when pressure-overload hypertrophy is induced in the right as well as the leftventricle. These studies were based on minimal coronary vascular resistance (MCVR) data (corrected for cardiac mass) obtained during maximal vasodilation accomplished by infusing adenosine, carbochrome, or dipyridamole. Such evidence has led to the conclusion that the total cross-sectional area of the resistance vessels during LVH secondary to hypertension does not increase in proportion to the muscle mass. However, insufficient growth of coronary vessels is but one explanation for the observed increased MCVR. Chronic pressure elevation might promote vascular changes (e.g., vascular stiffness or increased wall/lumen ratio or both) that might limit vasodilation.

Recently, we demonstrated that left ventricular MCVR in spontaneously hypertensive rats (SHR) became significantly elevated as hypertension persisted and hypertrophy progressed. However, right ventricular MCVR also increased with time despite the absence of hypertrophy. Since the increase in resistance was absent in 3-month-old SHR even though they had attained hypertensive blood pressure levels, the data suggest that the increase in resistance in SHR is a consequence of long-term hypertension.
To test this hypothesis, we prevented the characteristic rise in blood pressure in SHR by chronic administration of the peripheral vasodilator hydralazine. Despite the efficacy of this agent in maintaining normotensive blood pressure levels, it has little effect on the development of LVH. Thus, we were able to prevent hypertension without precluding LVH. The right ventricle served as an internal control since its vasculature is exposed to the same pressures but is not subjected to the intergroup differences in afterload evident for the left ventricle.

Materials and Methods

Animals and Protocol

The data are based on 27 male Wistar-Kyoto rats (WKY) and SHR bred at the University of Iowa Cardiovascular Center. When the rats were 1 month of age, the two strains were randomly divided into treatment and control groups. All treated animals received hydralazine (Ciba-Geigy Corp., Summit, NJ, USA), 80 to 100 mg per liter of drinking water, during a 6- to 7-month period. Blood pressures were recorded by the tail cuff method at least biweekly. The prolonged treatment period encompassed the development of hypertension and LVH and the attainment of elevated MCVR.

At the conclusion of the treatment period the animals were instrumented under sodium pentobarbital anesthesia (50 mg/kg i.p.). Instrumentation consisted of implanting catheters into the right and left femoral arteries, right jugular vein, and the left ventricle (retrograde) through the right common carotid artery. Details of this procedure have been described previously. The rats were allowed to regain consciousness and were studied on the next day. At the time of study the treated SHR and WKY had not received hydralazine for 48 hours. This was done so that the acute effects of the vasodilator would not affect the data. We obtained hemodynamic and myocardial blood flow data from six control WKY, eight treated WKY, six control SHR, and seven treated SHR.

All measurements were made on conscious, unrestrained rats. We monitored arterial pressure and heart rate with an Alitech MS20 transducer (City of Industry, CA, USA) and recorded these data on an oscillographic recorder. Blood gas and hematocrit values were determined in 0.3-ml blood samples. An equal volume of strain-matched donor blood was infused immediately following withdrawal.

Radioactive microspheres were injected into the left ventricle through the carotid cannula to measure myocardial perfusion at three different times as previously described. The first batch of microspheres was injected to determine perfusion at rest. Subsequently, maximal vasodilatation was induced by infusing dipyridamole with an infusion pump. A 2 mg/kg/min dose, previously shown to evoke maximal coronary vasodilatation, was infused for 10 minutes; microspheres labeled with a third radioisotope were then injected, and dilator infusion continued for another 2 minutes. After hemodynamic parameters had stabilized, a second dose of dipyridamole (4–8 mg/kg/min) was administered and microspheres labeled with a second radioisotope were injected. The second larger dose of dipyridamole was given to ensure that maximal vasodilation occurred in all animals. At the conclusion of the experiment, the heart was perfused with a glutaraldehyde fixative as previously described. The heart subsequently was removed, weighed, and dissected into segments (as described in the next section) for counting of radioactivity.

Measurement of Myocardial Perfusion

Radioactive microspheres (8–10 μm in diameter) labeled with 141Ce, 85Sr, or 65Sc were employed to measure regional myocardial perfusion (blood flow). This method has been recently described in detail. Only a brief description is included here.

Two reference blood samples were obtained simultaneously through the two femoral lines at a rate of 0.2 ml/min. Blood was withdrawn continuously before, during, and after microsphere injection and was immediately replaced with an equal volume of strain-matched donor blood. For each determination, approximately 5 × 10^6 microspheres was injected. Shunting of microspheres of this small size is negligible, and hemodynamics are not affected by microsphere injection.

To assess regional myocardial perfusion we dissected the left ventricle into four segments: (1) subepicardial and (2) subendocardial halves of the free wall and (3) left and (4) right halves of the interventricular septum. The right ventricle constituted the fifth tissue sample. These five specimens, along with the two reference samples, were counted in a gamma counter for 10 minutes. Data from the counter were recorded on paper tape and processed with a PDP-11 computer (Hewlett-Packard, Palo Alto, CA, USA). Standard techniques were employed for isotope separation.

Myocardial perfusion was calculated using the formula myocardial perfusion = (Cm × 100)BFr/Cr, where Cm = counts per gram of myocardium, BFr = the rate of withdrawal from the reference arteries, and Cr = counts in the reference blood sample. Coronary vascular resistance was calculated by dividing mean arterial pressure by coronary flow.

If the counts in the reference samples differed by more than 20% the flow data were discarded; this occurred in four measurements. The mean difference (± SEM) between the reference samples used in this study was 5.6 ± 0.6%. We also compared myocardial perfusion of the anterior and posterior halves of the epicardial samples of the left ventricle to verify sufficient mixing of microspheres in the coronary circulation. The mean (± SEM) of the differences for these samples was 5.1 ± 1.2%.

Histological and Morphometric Methods

After the radioactivity had been counted, tissue specimens were dissected from the epicardial half of left ventricular samples. These specimens, which in-
Hydralazine treatment in SHR maintained blood pressure levels within the normotensive range throughout the experimental period (Figure 1). Monthly means for systolic blood pressure ranged from 115 to 133 mm Hg in the treated SHR compared with 168 to 191 mm Hg in the nontreated SHR and 111 to 122 mm Hg in the nontreated WKY. Thus, blood pressures in the treated SHR were similar to those of the WKY. In treated WKY, blood pressures ranged between 99 and 107 mm Hg and were also significantly lower than their nontreated controls (p < 0.05).

A significant LVH was evident in SHR on the basis of both absolute left ventricular weights and left ventricular weight/body weight ratios (p < 0.05; Table 1). Hydralazine treatment had a minimal effect on LVH; absolute left ventricular weight and left ventricular weight/body weight ratio differences between the treated and nontreated SHR did not attain statistical significance. Therefore, while hydralazine prevented the development of hypertension, cardiac hypertrophy in SHR was not precluded despite the long-term treatment.

Hemodynamics
Heart rates were similar for all four groups at rest and increased by 26 to 37% during the infusion of dipyridamole (Table 2). Hypertensive blood pressure levels, as indicated by mean arterial pressures, were evident both at rest and during maximal vasodilation in the SHR (see Table 2). In the hydralazine-treated SHR, blood pressures were significantly lower than the nontreated SHR both at rest and during maximal vasodilation (p < 0.05), despite the fact that drug treatment was discontinued 48 hours before the determination of hemodynamics and myocardial perfusion. Mean arterial blood pressure in all groups tended to be slightly lower during dipyridamole infusion than at rest.

Intergroup differences for blood gas, pH, and hematocrit values were not observed either at rest or during vasodilation. The values for these parameters were within the normal physiological range.

Myocardial Perfusion
Myocardial perfusion data for the left and right ventricles are provided in Table 2. None of the mean differences between groups were significant for left ventricular perfusion either at rest or during maximal vasodilation, whether expressed as total perfusion or perfusion per 100 g of ventricle. The ratio of perfusion of the inner and outer portions of the ventricular free wall (subendocardium and subepicardium respectively) approximated unity in all groups at rest. The maximal vasodilation was characterized by a reduction in the subendocardial/subepicardial ratio; however, the intergroup differences for this ratio were not significant at rest or during maximal vasodilation.

Significant intergroup differences in right ventricular perfusion did not occur at rest. During maximal vasodilation, however, the values were higher in treated SHR than in control SHR, and differences between these two groups were significant when data were expressed as total perfusion or when expressed as perfusion per 100 g of ventricle.

Coronary Vascular Resistance
Calculated coronary vascular resistance for the left and right ventricles at rest did not differ significantly between the four groups (Table 3). In contrast, several
TABLE 1. Body and Heart Weight

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Body (g)</th>
<th>Left ventricle (mg)</th>
<th>Left ventricle/body (mg/g)</th>
<th>Right ventricle (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wistar-Kyoto rats</strong></td>
<td>Control</td>
<td>Treated</td>
<td>Control</td>
<td>Treated</td>
</tr>
<tr>
<td>Body (g)</td>
<td>381 ±14</td>
<td>384 ±12</td>
<td>381 ±13</td>
<td>373 ±14</td>
</tr>
<tr>
<td>Left ventricle (mg)</td>
<td>912 ±37</td>
<td>895 ±32</td>
<td>1121 ±32*</td>
<td>1014 ±34</td>
</tr>
<tr>
<td>Left ventricle/body (mg/g)</td>
<td>2.39 ±0.09</td>
<td>2.34 ±0.07</td>
<td>2.95 ±0.07*</td>
<td>2.73 ±0.08</td>
</tr>
<tr>
<td>Right ventricle (mg)</td>
<td>188 ±10</td>
<td>204 ±8</td>
<td>188 ±9</td>
<td>202 ±9</td>
</tr>
</tbody>
</table>

Values are means ± SEM.

SHR = spontaneously hypertensive rats.

*p ≤ 0.05, statistically significant differences between groups, SHR versus Wistar-Kyoto rats.

TABLE 2. Hemodynamics and Myocardial Perfusion at Rest and During Maximal Vasodilation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Status</th>
<th>Wistar-Kyoto rats</th>
<th>SHR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Control</td>
<td>Treated</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>Rest</td>
<td>328 ±17</td>
<td>303 ±12</td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>441 ±8</td>
<td>418 ±8</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>Rest</td>
<td>107 ±5</td>
<td>99 ±4</td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>98 ±7</td>
<td>79 ±7</td>
</tr>
<tr>
<td>Myocardial perfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total perfusion (ml/min)</td>
<td>Rest</td>
<td>3.45 ±1.08</td>
<td>2.86 ±0.76</td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>8.21 ±0.91</td>
<td>10.33 ±0.85</td>
</tr>
<tr>
<td>Perfusion (ml/min) per 100 g</td>
<td>Rest</td>
<td>408 ±116</td>
<td>360 ±82</td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>994 ±107</td>
<td>1269 ±98</td>
</tr>
<tr>
<td>Subendocardium/subepicardium ratio</td>
<td>Rest</td>
<td>1.26 ±0.18</td>
<td>1.06 ±0.12</td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>0.71 ±0.06</td>
<td>0.75 ±0.06</td>
</tr>
<tr>
<td>Right ventricle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total perfusion (ml/min)</td>
<td>Rest</td>
<td>0.47 ±0.23</td>
<td>0.48 ±0.19</td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>1.94 ±0.19</td>
<td>2.29 ±0.17</td>
</tr>
<tr>
<td>Perfusion (ml/min) per 100 g</td>
<td>Rest</td>
<td>227 ±116</td>
<td>193 ±82</td>
</tr>
<tr>
<td></td>
<td>MVD</td>
<td>1034 ±95</td>
<td>1135 ±88</td>
</tr>
</tbody>
</table>

Values are means ± SEM.

MAP = mean arterial pressure; MVD = minimal vasodilation; SHR = spontaneously hypertensive rats.

*p ≤ 0.05 (treated vs strain control), †p ≤ 0.05 (SHR vs WKY), statistically significant differences between groups.

TABLE 3. Coronary Vascular Resistance (CVR) at Rest

<table>
<thead>
<tr>
<th>CVR (mm Hg/ml/min)</th>
<th>Wistar-Kyoto rats</th>
<th>SHR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Treated</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>Per 100 g</td>
<td>0.52 ±0.12</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>271 ±65</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>Per 100 g</td>
<td>0.28 ±0.11</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>34 ±15</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.

None of the differences between groups are statistically significant (p ≤ 0.05).

SHR = spontaneously hypertensive rats.

significant differences between groups were noted for MCVR (Figures 2 and 3). For the left ventricle, MCVR per 100 g of tissue was significantly higher in SHR than in WKY. Chronic hydralazine treatment markedly reduced MCVR (per 100 g of tissue) in both SHR and WKY. Although total left ventricular MCVR in SHR did not differ significantly from WKY, hydralazine treatment in both strains significantly reduced total MCVR (by 37% in WKY and by 33% in SHR; p < 0.01).

The MCVR per 100 g of tissue in the right ventricle was also significantly higher in SHR than in WKY (p < 0.002). As in the left ventricle, right ventricular MCVR per 100 g of tissue in SHR was markedly
SHR were similar to those of WKY whether expressed as total MCVR or MCVR per 100 g of ventricle. Antihypertensive treatment also affected WKY, as evidenced by a significant reduction in total left ventricular MCVR, as well as MCVR per 100 g of tissue (p < 0.01).

Histological data are illustrated in Figure 4. Wall/lumen ratios of coronary arterioles and small arteries (with diameters < 200 μm) were generally larger in decreased (47%) after chronic hydralazine treatment. Total right ventricular MCVR, which was also elevated in SHR compared with WKY, decreased by 51% with antihypertensive treatment. In treated WKY, both MCVR per 100 g of tissue and total MCVR were lower than that found in the control WKY, but the differences did not attain statistical significance.

In summary, the data shown in Figures 2 and 3 indicate that when hypertension in SHR was prevented with hydralazine, MCVR was decreased in the right as well as the left ventricle. The values for the treated
SHR than in WKY. Compared with their controls hydralazine-treated SHR tended to have smaller wall/lumen ratios. In contrast, treatment of WKY did not appear to reduce wall/lumen ratio. As the following list shows, capillary density was not affected by hydralazine treatment in either strain. The values shown represent the number of capillaries per square millimeter (mean ± SEM).

<table>
<thead>
<tr>
<th>Group</th>
<th>Capillaries/mm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>WKY</td>
<td>4094 ± 203</td>
</tr>
<tr>
<td>Treated WKY</td>
<td>3990 ± 186</td>
</tr>
<tr>
<td>SHR</td>
<td>3576 ± 186</td>
</tr>
<tr>
<td>Treated SHR</td>
<td>3645 ± 161</td>
</tr>
</tbody>
</table>

The differences between the treated and nontreated groups are not statistically significant.

Discussion

This study provides evidence that the increased MCVR, which becomes evident between the third and seventh months of life in SHR, is not due to a genetic strain variation nor is it secondary to myocardial hypertrophy but rather is associated with the persistence of elevated blood pressure. Our conclusions are based on data showing that both total MCVR and MCVR per 100 g of tissue are normal in both ventricles when hypertension is prevented in SHR.

Previous studies have indicated that pressure overload and LVH in dogs are associated with a decrement in coronary vasodilator reserve. This suggestion is based on evidence that the left ventricles of these dogs show a decrease in the endocardial to epicardial blood flow ratio during reactive hyperemia and exercise and that MCVR, induced by pharmacological vasodilation, is increased. Since both LVH and systemic hypertension were present in these dogs, the role of each variable in coronary circulation deficits could not be defined. The assessment of total MCVR during maximal vasodilation serves to estimate the functional cross-sectional area of the coronary bed. Because total MCVR was unchanged and MCVR per 100 g of tissue increased in the hypertrophied left ventricle of dogs with hypertension it was concluded that the functional cross-sectional area of the coronary bed does not increase with hypertrophy. Such a conclusion is also supported by a recent study on renovascular hypertensive rats. However, O’Keefe et al. found that MCVR per gram of tissue approximately doubled in the right ventricle of dogs with left ventricular pressure overload. Although the presence of a mild right ventricular hypertrophy precluded definitive conclusions, these authors suggested that the role of coronary artery changes in direct response to a high systolic pressure deserves consideration.

Further support for our conclusion is the evidence that total MCVR decreases and MCVR per 100 g of tissue is unchanged in dogs with volume-overload LVH. These findings indicate that, unlike pressure-overload hypertrophy, vascular growth keeps pace with increases in myocardial mass in this model of hypertrophy. Thus, the vascular responses in these two models of LVH are in sharp contrast.

Our data implicate blood pressure in the decrease in functional cross-sectional area of the vascular bed. This conclusion is based on several lines of evidence. First, we confirmed our previous finding that compared with that in WKY, the nonhypertrophied right ventricle of 7-month-old SHR has a significantly higher MCVR per 100 g of tissue. Moreover, total right ventricular MCVR in SHR was also markedly elevated compared with that in WKY. Second, when hypertension was prevented in SHR, right ventricular MCVR per 100 g of tissue was virtually identical to that of WKY, despite an unchanged ventricular mass. That the absolute functional cross-sectional area of the right ventricular coronary bed of treated SHR was greater than that of nontreated SHR is indicated by the considerably lower total MCVR for the treated group. Thus, the total cross-sectional area of the coronary bed in SHR that never experienced hypertension was the same as that in their genetic normotensive controls. Third, both total MCVR and MCVR per 100 g of tissue in the left ventricle were significantly lower in treated than in nontreated SHR and similar to those of the control WKY. The finding that LVH was not as marked after hydralazine treatment in SHR does not explain the normalization of MCVR. A significantly lower total left ventricular MCVR indicates that the functional cross-sectional area of the coronary vasculature was greater when hypertension was prevented in SHR. If a change in left ventricular mass played a role then one would expect that antihypertensive treatment would effect a lower MCVR per 100 g of tissue but would not alter total MCVR in the left ventricle. Finally, the decrease in total MCVR in the left ventricle of WKY suggests that even a modest reduction in blood pressure was associated with an increase in functional cross-sectional area of the coronary vascular bed.

A recent review concerning resistance vessel abnormalities and elevated blood pressure in SHR concludes that many factors may contribute to the increased total peripheral resistance. Evidence for a general constriction of the vasculature (due to functional or structural abnormalities) and rarefaction of the vascular bed is cited. If such factors are present in the coronary vasculature of SHR they do not elevate resistance at rest, which suggests that myocardial perfusion increases in proportion to the hypertension. That MCVR was higher in SHR suggests a decrease in vasodilator reserve that could be due to vascular rarefaction or limitations in the maximal dilatory response of the resistance vessels. The latter could be a consequence of either structural or functional alterations in these vessels.

A common explanation for the finding of increased MCVR is that structural alterations have occurred in the vascular tree. Hyperplastic lesions in coronary arteries in rats with renovascular hypertension and a decreased wall/lumen ratio in coronary arterioles of SHR have been reported. A study on epicardial arteries in SHR revealed that the ultrastructural alterations...
in these vessels, which include medial accumulation of collagen and debris, are progressive and cumulative.24 Degenerative changes, however, did not appear during the first 3 months of life. These observations may explain why MCVR in SHR, as previously shown, is trend toward lower values in treated SHR than in non-treated SHR. Since resistance is inversely related to the fourth power of the vessel’s radius, a small increase in wall thickness would have a marked impact on resistance. Therefore, the influence of hydralazine on MCVR in SHR may have been due at least in part to minimizing the increase in wall thickness associated with hypertension. However, our histological data are not conclusive, largely due to infrequency of resistance vessels in tissue sections and the variability of wall/lumen ratios. Therefore, this method was not sufficiently sensitive for the discernment of small differences between groups.

Our histological data on wall/lumen ratios shows a trend toward lower values in treated SHR than in non-treated SHR. This conclusion is further supported by our data on treated WKY. It is possible that hydralazine treatment in SHR precluded some functional change in the vascular smooth muscle of the coronary resistance vessels. That the increase in resistance to coronary flow in SHR during maximal vasodilation occurs in combination with an increased maximal constrictor response has been demonstrated.25 Although hydralazine does not reverse medial hypertrophy in the aorta26 or decrease collagen synthesis in the mesenteric arteries,23 it does reduce the force-generating ability of the aorta.25 Another possible explanation for the increased MCVR in SHR is an absolute decrease in the number of resistance vessels. A rarefaction of microvessels in skeletal muscle of SHR has been suggested as a mechanism of blood flow regulation in response to tissue overperfusion during the development of hypertension.27 Our finding that total MCVR in both ventricles was lower in hydralazine-treated than in control SHR is also consistent with this possibility.

The decline in MCVR in treated WKY is obviously not related to the prevention of increased wall thickness. Since chronic treatment with the vasodilator did decrease blood pressure, intravascular mechanical forces would also be reduced, which might modify the vessel’s distensibility. A recent study has shown that chronic lowering of blood pressure in normotensive WKY prevents the age-related thickening of the subendothelial space of the aorta.28 Another possibility is that resistance vessel cross-sectional area increased by an increase either in the number of vessels or in luminal diameter. Although the present study did not address vascular mechanisms that might modulate MCVR, our data indicate that the elevated MCVR in SHR was due to factors associated with chronic hypertension. We conclude that a similar decrement in coronary reserve develops in both ventricles with persistent hypertension and can be corrected by preventing the hypertension. These conclusions currently are limited to SHR and should not be extrapolated to other models of hypertension and LVH. Nevertheless, the findings of this study suggest that long-term hypertension may compromise coronary reserve even in the absence of cardiac hypertrophy. That MCVR is related to blood pressure levels is further supported by our data on treated WKY.

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References


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