Left Ventricular Blood Flow During Aortic Pressure Reduction in Hypertensive Dogs

Joseph J. Smolich, Peter L. Weissberg, Peter Friberg, Archer Broughton, and Paul I. Korner

We measured left ventricular blood flow with radioactive microspheres during aortic pressure reduction in 10 open-chest, anesthetized dogs with left ventricular hypertrophy due to chronic hypertension and in 10 matched normotensive dogs. Heart rate and left atrial pressure were held constant, and autonomic reflexes were abolished with ganglionic blockade. Aortic diastolic pressure was lowered from baseline to 90, 75, and 60 mm Hg with an arteriovenous fistula. During aortic pressure reduction, a stepwise decline in the endocardial-to-epicardial flow ratio in hypertrophied hearts from 1.23 ± 0.04 at baseline to 0.96 ± 0.09 at a diastolic pressure of 75 mm Hg paralleled that in normal hearts and was not associated with any deterioration in left ventricular performance. However, a further fall in the endocardial-to-epicardial flow ratio to 0.76 ± 0.10 at a diastolic pressure of 60 mm Hg in hypertrophied hearts exceeded that in normal hearts (0.92 ± 0.05, p < 0.05) and was accompanied by evidence of left ventricular isovolumic and end-systolic dysfunction. We conclude that in hearts with pressure-overload left ventricular hypertrophy, aortic pressure reduction causes a transmural blood flow redistribution from subendocardial to subepicardial muscle layers. At moderately low aortic pressures, this redistribution is more pronounced than in normal hearts and is associated with functional evidence of myocardial ischemia. (Hypertension 1991;18:665–673)

Several lines of evidence suggest that lowering aortic blood pressure in the setting of chronic hypertension may have deleterious effects on the heart. Experimental studies have demonstrated that in hearts with hypertension-induced left ventricular (LV) hypertrophy, LV isovolumic indexes and pump function are impaired at reduced aortic pressure levels that are well-tolerated by normal hearts. These findings are in accord with clinical studies that have noted either asymptomatic electrocardiographic changes or overt symptoms of myocardial ischemia after acute pressure reduction in hypertensive patients. Moreover, epidemiological studies that have described a U-shaped or J-shaped relation between the level of blood pressure after treatment and the incidence of cardiac mortality have led to the suggestion that excessive reduction of blood pressure with antihypertensive therapy might precipitate myocardial ischemia and infarction.

Since animal studies using electrical pacing and coronary artery constriction have shown that the hypertrophied left ventricle is susceptible to subendocardial perfusion deficits, one possible explanation for any detrimental effects of aortic pressure reduction in hypertrophied hearts is an alteration in LV transmural blood flow patterns. We have previously shown that in normal hearts, moderate aortic pressure reduction redistributes LV blood flow from subendocardial to subepicardial muscle layers, without depression of LV isovolumic indexes or electrical evidence of myocardial ischemia. It is not known, however, if aortic pressure reduction similarly redistributes LV transmural flow in hypertrophied hearts and if differences in the extent of any redistribution are apparent at a level of aortic pressure associated with LV functional impairment. Accordingly, the aim of the present study was to compare LV transmural blood flow responses during acute aortic pressure reduction in normotensive dogs and those with well-compensated LV hypertrophy due to renovascular hypertension.

Methods

The study was performed in 20 conditioned adult male mongrel dogs. Ten had LV hypertrophy secondary to chronic renovascular hypertension and 10 were normotensive dogs with a similar range of body weights.

Induction of Hypertension

One-kidney renovascular hypertension was produced as previously described. Briefly, the left
renal artery was exposed through a left flank incision under general anesthesia and instrumented with an inflatable Silastic cuff (Hazem Everett, Teaneck, N.J.) and a continuous wave Doppler probe (Baker Institute, Melbourne, Australia). Indwelling polyvinyl catheters (0.86 mm i.d., 1.52 mm o.d.) were inserted into the abdominal aorta for measurement of blood pressure. The right kidney was removed during the same surgical procedure through a right flank incision. Postoperatively, animals received analgesia as necessary and daily oral antibiotics during the 10–14 days required for complete recovery from surgery. Aortic blood pressure was then measured at regular intervals with the animals fully conscious and lying unrestrained on a padded table. The renal artery cuff was progressively inflated over several weeks to produce a gradual increase in arterial blood pressure, which was then maintained for at least 7 weeks.

**Experimental Preparation**

Normotensive and hypertensive dogs were anesthetized with intravenous sodium pentobarbitone (25 mg/kg bolus followed by a constant infusion of 6 mg/kg/hr), intubated, and artificially ventilated at an end-expiratory pressure of 4 cm H₂O with oxygen-enriched room air. Arterial blood gas samples were analyzed frequently (Radiometer ABL1, Copenhagen, Denmark), and ventilation was adjusted to maintain arterial carbon dioxide tension between 35 and 40 mm Hg and pH between 7.3 and 7.4. Sodium bicarbonate was administered, as necessary, to correct any base deficits. Rectal temperature was kept between 36° and 38°C with a heated table and a thermostatically controlled water blanket. The surgical preparation was as described previously. Briefly, the chest was opened in the fourth or fifth left intercostal space, and a high-fidelity micromanometer (model P 4.5, Konigsberg Instruments, Oxnard, Calif.) was inserted through the cardiac apex to record LV pressure. A large bore cannula, connected to a reservoir, was inserted into the left atrial cavity to control mean left atrial pressure. The reservoir was filled with room-temperature heparinized whole blood, obtained from a donor dog and diluted approximately 4:1 with 10% dextran in normal saline. Fluid-filled catheters were passed into the left atrium and the aortic arch for pressure measurement. All pericardial incisions were closed with interrupted sutures. An arteriovenous (AV) fistula was constructed between the thoracic aorta and an external jugular vein with wide-bore tubing, and its flow was regulated by a roller pump. Unipolar endocardial and epicardial electrodes were also inserted in three hypertensive and five normal dogs.

**Experimental Protocol**

The cervical vagosympathetic trunks were cut and autonomic ganglia blocked with mepacrine (2 mg/kg i.v.) to eliminate reflex changes in LV contractility resulting from aortic pressure reduction. The adequacy of autonomic blockade was confirmed by the absence of changes in heart rate and LV isovolumic indexes in response to a 60-second bilateral carotid occlusion. After autonomic blockade, the heart was paced at 150 beats/min with a stimulator (model SD9, Grass Instrument Co., Quincy, Mass.) and a bipolar left atrial electrode. Open-chest mean left atrial pressure was maintained constant at 15 mm Hg, which is at the upper limit of normal.

Hemodynamic indexes and two-dimensional echocardiographic (2-D echo) LV images were recorded, and LV blood flow was measured with radioactive microspheres under baseline conditions. Aortic diastolic pressure (ADP) was then reduced stepwise from the baseline value to approximately 90, 75, and 60 mm Hg with the AV fistula. Hemodynamic, 2-D echo, and blood flow measurements were repeated at each reduced pressure level after steady-state conditions had been maintained for 3–5 minutes. In about half of the dogs, hemodynamics and 2-D echo images were also recorded at other intermediate pressures between baseline and ADP 60 mm Hg.

In five normotensive and five hypertensive dogs blood pressure was reduced below ADP 60 mm Hg in steps of approximately 10 mm Hg until the development of ischemic changes in the endocardial electrogram or obvious echocardiographic LV dilatation. Hemodynamic measurements and recording of 2-D echo images were repeated at each pressure level.

At the end of the experiment, the dogs were killed with an overdose of sodium pentobarbitone and potassium chloride. The hearts were removed and immersed in fixative for 7–10 days.

**Hemodynamic Measurements**

Aortic and left atrial pressures were measured with strain gauge transducers (model P23D, Statham Instruments, Oxnard, Calif.), using the midthoracic vertebral spines as the zero reference level. The isovolumic indexes dP/dtiso (the maximal rate of rise of LV pressure) and dP/dtmax (the rate of rise of LV pressure at a developed pressure of 40 mm Hg) were obtained from a differentiator having a linear output (±5%) up to a frequency of 90 Hz. LV, aortic, and left atrial pressures were monitored with an eight-channel paper recorder (model M19, Devices Limited, Welwyn Garden City, England) and were recorded on a multichannel tape recorder (model 3960 or 3968A, Hewlett-Packard, Palo Alto, Calif.) for subsequent analysis.

**Measurement of Myocardial Blood Flow**

LV blood flow was measured with approximately 1 million 15-μm radioactive microspheres labeled with one of six randomly chosen labels (¹⁴¹Ce, ⁵¹Cr, ¹¹³Sn, ⁸⁸Sr, ⁹⁹Nb, and ⁴⁶Sc; New England Nuclear, Boston, Mass.). The microspheres were mixed for 10 minutes by ultrasonification and manual agitation and were flushed into the left atrial cavity over 30–40 seconds with 15 ml saline. A reference sample was withdrawn at a constant rate of 12 ml/min from an aortic catheter with a mechanical pump (model
940A, Harvard Apparatus, South Natick, Mass.), starting 5–10 seconds before injection and ending 75–90 seconds after injection.

The aorta, great arteries, epicardial fat, large coronary vessels, valves, and right ventricular free wall were removed from the fixed hearts. The left ventricle was divided into subendocardial, inner midwall, outer midwall, and subepicardial layers. This dissection yielded 84 separate tissue samples. In normal dogs, the subendocardium, inner midwall, outer midwall, and subepicardium comprised 25.0±0.5 (mean±SEM), 19.6±0.3, 21.8±0.4, and 33.6±0.8%, respectively, of total LV weight. The corresponding proportions for the hypertensive dogs were 24.3±0.3, 19.2±0.2, 21.4±0.3, and 35.1±0.7%.

The radioactivity of the reference and tissue samples was measured in a through-hole gamma counter (model 5130, Packard Instrument Co., Downer’s Grove, Ill.). The radioactivity of each isotope peak in the tissue samples was obtained by stripping away the contribution of background and the Compton areas of higher energy isotopes with a computer program. Blood flow was calculated from the relation:

\[ Q_{\text{Tissue}} = Q_{\text{Reference}} \times R_{\text{Tissue}} / R_{\text{Reference}} \]

where \( Q \) is flow (ml/min) and \( R \) is radioactivity (counts/min). In each animal, subendocardial, inner midwall, outer midwall, subepicardial, and total LV blood flows were obtained by appropriate summation of the individual sample flows. All flows were normalized to 100 g of wet tissue.

Two-dimensional Echocardiography

LV 2-D echo views were obtained with a 5 MHz medium focus phased-array transducer and 77020AC ultrasound system (Hewlett-Packard, Andover, Mass.). For each view, stop-frame images were triggered with a surface electrocardiogram at two instances in the cardiac cycle. The first was at the point of positive dP/dt. As positive dP/dt occurs well before aortic valve opening in our preparation, LV dimensions at this instant were assumed to be equivalent to those at end diastole. The second was at 20 msec before negative dP/dt, which corresponds to LV end systole (more precisely, end ejection).

Satisfactory end-systolic LV major and minor axis images were obtained in eight normotensive dogs and in all 10 hypertensive animals.

LV dimensions were obtained directly from videotape recordings with an onboard analysis program, using the trailing-leading edge method to define endocardial and epicardial outlines. Average LV wall thickness was calculated as the difference between the equivalent radii of the minor axis internal (\( A_i \)) and external cross-sectional areas. The length of the major axis (L) was measured between the cardiac apex and a point lying midway along the plane of the mitral valve annulus. The left ventricle was assumed to have prolate ellipsoid geometry so that LV cavity volume equaled \( 2/3 \times A_i \times L \).

**End-systolic Pressure–Volume and Wall Stress–Volume Relations**

The pressure volume points at end systole were fitted to the line of best fit using least-squares linear regression. The slope of this relation, the end-systolic elastance (\( E_s \)), is a measure of LV systolic chamber function that is relatively independent of cardiac loading conditions. This is an advantage over isovolumic indexes, which become quite load dependent at lower aortic pressures. The end-systolic pressure–volume relation was obtained during stepwise lowering of aortic blood pressure with the AV fistula. As mean left atrial pressure was held constant during this intervention, LV end-diastolic volume underwent only minor changes. However, stroke volume increased, and LV end-systolic volume therefore decreased. The number of points used to construct an end-systolic pressure–volume relation ranged between four and seven in the hypertensive dogs and four and six in the normal animals, each point representing a different steady-state level of aortic pressure. LV end-systolic pressure was assumed to be equivalent to aortic dicrotic notch pressure. LV volume at each point was calculated using the average of the 2-D echo LV minor axis cross-sectional area and major axis length measurements from five cardiac cycles.

To assess myocardial properties in normotensive and hypertensive dogs, the corresponding end-systolic wall stress–volume relation was calculated using the formula for a prolate ellipsoid. Circumferential wall stress, the major component of LV wall stress, was thus equivalent to

\[ 1.36[P-D/4H][(2L^2-D^2)/(L^2+D-H)] \]

where \( P \) is aortic dicrotic notch pressure (mm Hg), \( D \) is minor axis internal diameter (mm), \( L \) is major axis dimension (mm), \( H \) is wall thickness (mm), and 1.36 is the conversion factor (mm Hg to g/cm²).

**Statistical Analysis**

Results were analyzed with standard statistical tests. The effect of blood pressure reduction on LV blood flow and isovolumic indexes was assessed with two-way and three-way analysis of variance. The between-pressures and, with the blood flow data, the between-regions sums of squares were orthogonally partitioned into individual degrees of freedom. Significant differences between normotensive (N) and hypertensive (HT) dogs during aortic pressure reduction were assessed from

\[ t = \Delta(HT-N)/(SE_N^2+SE_{HT}^2)^{0.5} \]

with \( (n_N+n_{HT}-2) \) degrees of freedom, where \( \Delta(HT-N) \) is the difference between the response of the hypertensive and normal dogs and \( SE \) is the appropriate standard error from each analysis of variance. Differences in the end-systolic pressure–volume and end-systolic wall stress–volume relations between normotensive and hypertensive dogs were evaluated with
analysis of covariance, using pooled regression coefficients calculated for each group. Unless otherwise stated, results are expressed as mean±SEM. A value of p<0.05 was considered significant.

Results

Baseline Characteristics

Mean arterial blood pressure increased from 100±3 mm Hg to 129±4 mm Hg (p<0.005) with progressive renal artery constriction. This level of hypertension was maintained for an average of 10 weeks (range, 7–16 weeks). Serum creatinine, measured at the end of this time in six hypertensive dogs, was 0.10±0.01 mmol/l (normal range 0.07–0.13 mmol/l). Hemoglobin level in the hypertensive dogs (13.1±0.5 g/dl, n=10) was similar to that in normotensive animals (13.9±0.4 g/dl, n=6).

End-diastolic LV minor axis diameter, measured with 2-D echocardiography under baseline conditions during the acute experiment, was similar in normotensive and hypertensive dogs. However, LV weight, the LV weight-to-body weight ratio, LV wall thickness, and LV wall-to-lumen ratio were between 23% and 34% greater in the hypertensive dogs (Table 1).

Hemodynamics and Isovolumic Indexes

Compared with normal dogs, resting aortic blood pressures were approximately 25% higher in the hypertensive dogs, but matched at the reduced pressure levels (Table 2). In normal dogs, dP/dt_{max} decreased by 5% (p<0.05) at ADP 60 mm Hg, but dP/dt_{DP40} was similar throughout the pressure reduction (Table 2). In hypertensive dogs, dP/dt_{max} was initially maintained with lowering of aortic blood pressure but then fell by 15% at ADP 60 mm Hg (p<0.005). The latter decline was greater than in normotensive dogs (p<0.025) and was accompanied by a 10% decrease in dP/dt_{DP40} (p<0.005) (Table 2).

Left Ventricular Myocardial Blood Flow

Under baseline conditions, total LV blood flow in hypertensive dogs, 238±37 ml/min, was higher than in normotensive animals, 144±17 ml/min (p<0.05, unpaired t test), but a difference was not apparent when...
FIGURE 1. Plots show changes in average left ventricular (LV) blood flow (panel A), transmural LV blood flow (panel B), transmural LV blood flow as a percentage of control flow (panel C), and the endocardial-to-epicardial (Endol Epi) flow ratio (panel D) during aortic pressure reduction in normotensive and hypertensive dogs. EN, subendocardium; EP, subepicardium. Error bar equals 1 SE of the difference between any two means obtained from two- and three-way analysis of variance.

related in both normotensive ($r=0.950 \pm 0.013$, $n=8$) and hypertensive dogs ($r=0.966 \pm 0.009$, $n=10$). The regression coefficients of this relation (i.e., $E_{a}$) ranged from 3.2 to 8.6 mm Hg/ml in normotensive dogs and from 4.2 to 17.3 mm Hg/ml in the hypertensive animals. Comparing the two groups, the pooled regression coefficient in the hypertensive dogs (6.4 $\pm$ 0.5 mm Hg/ml) was significantly greater than that of the normotensive dogs, 4.5 $\pm$ 0.5 mm Hg/ml ($p<0.025$) (Figure 2A). The corresponding LV circumferential end-systolic wall stress–volume relation was also linear in normotensive ($r=0.981 \pm 0.005$, $n=8$) and hypertensive dogs ($r=0.986 \pm 0.003$, $n=10$). However, in contrast to the end-systolic pressure–volume relation, the pooled regression coefficient in hypertensive dogs, 12.6 $\pm$ 0.6 g/cm²/ml was similar to that of normotensive animals, 12.4 $\pm$ 0.6 g/cm²/ml (Figure 2B).

With progressive reduction of aortic blood pressure, the LV pressure–volume points deviated strikingly from the regression line. Further decreases in aortic pressure then produced increases in the end-systolic volume (i.e., LV dilatation) (Figures 3 and 4). This departure from linearity of the LV pressure–volume points was observed at an aortic diastolic pressure of 33 $\pm$ 2 mm Hg in normotensive dogs.
Figure 2. Plots show pooled regression lines of left ventricular end-systolic pressure–volume (panel A) and circumferential wall stress–volume relations (panel B) in normotensive (N) and hypertensive (HT) dogs.

(n=5) and 57±5 mm Hg in the hypertensive animals (n=6, p<0.005, unpaired t test).

Discussion

Two main findings have emerged from this study. First, in hearts with LV hypertrophy secondary to chronic hypertension, aortic pressure reduction decreases mean LV blood flow and redistributes transmural LV flow from subendocardial to subepicardial muscle layers. Second, this transmural redistribution in hypertrophied hearts is more pronounced than in normal hearts at moderately low aortic pressures and is then associated with depression of LV isovolumic and end-systolic indexes.

Normal LV end-diastolic dimensions in association with a greater LV wall thickness and wall-to-lumen ratio (Table 1) suggested that the hypertensive animals in our study had well-compensated concentric LV hypertrophy. The greater slope of the end-systolic pressure–volume relation in hypertrophied hearts (Figure 2A) was consistent with an increase in global LV systolic function.20,21 By contrast, the identical slope of the end-systolic wall stress–volume relation in the two groups (Figure 2B) indicated that performance was similar per unit area of myocardium. This implies that the increased global LV systolic function in the hypertrophied hearts of our study was attributable to increases in LV wall thickness and wall-to-lumen ratio, in the absence of any enhanced performance of individual muscle units.

The latter notion is in accord with suggestions made in our previous study that characterized LV pump performance by the mean LV pressure–cardiac index relation15 and with the results of Sasayama et al24 on the compensated phase of LV hypertrophy after aortic constriction.

Our finding of a similar baseline LV flow per unit weight in hypertensive dogs is in agreement with
FIGURE 4. Minor axis two-dimensional echocardiographic views of the hypertrophied heart in Figure 3B. Upper panel: Image at the lower limit of the linear end-systolic pressure-volume relation (end-systolic pressure 100 mm Hg). Cross-sectional area of the left ventricular (LV) cavity is outlined by the dotted markers. Lower panel: Image after development of pronounced LV dilatation (end-systolic pressure 48 mm Hg), superimposed with the same area defined by markers in upper panel.

previous studies of LV pressure–volume overload hypertrophy. With aortic pressure reduction, average LV blood flow fell progressively in hypertrophied hearts suggesting that as in normal hearts, the metabolic cost of rises in cardiac output during aortic pressure reduction was far outweighed by the effect of associated decreases in LV wall stress. In agreement with other studies, the baseline LV endocardial-to-epicardial flow ratio was similar in normotensive and hypertensive animals. Reducing aortic diastolic pressure from 144 to 76 mm Hg in the hypertensive group of dogs produced a progressive decrease in the endocardial-to-epicardial flow ratio, signifying a redistribution of LV transmural blood flow from subendocardial to subepicardial muscle layers. On the basis of direct and indirect measurements of regional LV intramyocardial pressure, as well as computer modeling of transmural myocardial mechanics, we previously concluded that the transmural redistribution of LV blood flow in normotensive hearts during aortic pressure reduction was a physiological phenomenon related to nonuniform transmural changes in regional LV wall stress and metabolism. As the decrease in the endocardial-to-epicardial flow ratio during aortic pressure reduction in hypertensive dogs initially paralleled that in normotensive animals and was not associated with any evidence of LV dysfunction, it is likely that a similar process occurred in the hypertrophied hearts.

At an aortic diastolic pressure of about 60 mm Hg, the decline in the endocardial-to-epicardial flow ratio in hypertrophied hearts exceeded that in normal hearts. This greater decline in the endocardial-to-epicardial flow ratio was accompanied by significant reductions in the isovolumic indexes $dP/dt_{DP40}$ and $dP/dt_{t_{max}}$. Unlike normotensive dogs, where a small decline in $dP/dt_{DP40}$ coupled to an unchanged $dP/dt_{t_{max}}$ at a diastolic pressure of 60 mm Hg was due to early aortic valve opening before attainment of full isovolumic $dP/dt_{t_{max}}$, the simultaneous and more marked falls in $dP/dt_{DP40}$ and $dP/dt_{t_{max}}$ in hypertrophied hearts at the same pressure were consistent with a depression of inotropic state. The greater decline in the endocardial-to-epicardial flow ratio at a diastolic pressure of 60 mm Hg was also associated with the emergence of a departure of LV pressure–volume points from the linear end-systolic pressure–volume relation. This departure closely resembled that reported in isolated hearts during reductions in coronary perfusion pressure below the lower limit of coronary autoregulation, a pattern that was presumed to result from the movement of pressure–volume points onto linear end-systolic pressure–volume relations with lesser slopes. The changes in isovolumic and end-systolic indexes at an aortic diastolic pressure of 60 mm Hg in hypertrophied hearts of our study were thus both indicative of a deterioration in LV function, and therefore highly suggestive of the onset of myocardial ischemia.

A likely basis for the greater decrease in the endocardial-to-epicardial flow ratio observed at an aortic diastolic pressure of 60 mm Hg in the hypertensive dogs of our study was an alteration in coronary blood flow. In normotensive hearts, LV coronary blood flow is "autoregulated," that is, maintained within narrow limits over a wide range of coronary perfusion pressures by pressure-dependent alterations in vascular resistance. Below the lower pressure limit of autoregulation, LV blood flow falls with pressure reduction, accompanied by evidence of myocardial ischemia. Autoregulatory capacity also exhibits transmural differences, with loss of autoregulation occurring in the subendocardium at higher pressures than in the subepicardium. Several studies have now demonstrated that autoregulation of coronary blood flow is preserved in hearts with LV hypertrophy secondary to chronic hyperten-
sion, but that the lower limit of autoregulation is shifted to a higher pressure level. Moreover, the limited subendocardial vasodilator response elicited in renal hypertensive dogs either with a coronary stenosis or intravenous infusions of adenosine suggests that loss of autoregulation in the subendocardium also precedes that in the subepicardium in hypertrophied hearts.

We propose that the greater decline in the endocardial-to-epicardial flow ratio in hypertrophied hearts in our study at an aortic diastolic pressure of 60 mm Hg can be explained by a shift in the lower limit of coronary autoregulation to a higher pressure level, combined with loss of autoregulation in the subendocardium preceding that in the subepicardium. Thus, between the baseline state and an aortic diastolic pressure of about 75 mm Hg, we speculate that both subendocardial and subepicardial flows were autoregulated in hypertrophied hearts but more pronounced falls in subendocardial flow (which resulted in a declining endocardial-to-epicardial flow ratio) were due to greater reductions in subendocardial wall stress and metabolism. However, at an aortic diastolic pressure of 60 mm Hg, subepicardial flow was still autoregulated, but subendocardial flow was not because its pressure–flow point lay below the lower limit of subendocardial autoregulation. The fall in subendocardial flow was thus exaggerated, resulting in a relatively greater decrease in the endocardial-to-epicardial flow ratio. Since studies using ultrasonic crystals in hypertrophied hearts indicate that subendocardial underperfusion produces not only subendocardial but also transmural dysfunction, this hypothesis would also account for our finding of an association between an accentuated decline in the endocardial-to-epicardial flow ratio and global impairment of LV performance.

Clearly, there are limitations in extrapolating results obtained from anesthetized animal experiments conducted under highly controlled conditions to the clinical setting. However, our experimental findings support the clinical observations that acute lowering of aortic pressure can produce ischemic electrocardiographic changes in hypertensive patients without significant coronary artery disease at a pressure level without effect in normotensive patients. It has been presumed that these ischemic changes are due to subendocardial underperfusion. Our results suggest that such underperfusion could arise from an exaggeration of a redistribution of LV transmural blood flow toward subepicardial muscle layers normally accompanying aortic pressure reduction. Moreover, if this exaggerated redistribution is mainly related to a shift of the lower limit of coronary autoregulation to a higher pressure level, then the persistence of this shift in patients, despite long-term pressure normalization, may also in part explain the paradoxical increase in mortality observed with reduction of arterial diastolic pressure below about 90 mm Hg with antihypertensive therapy.

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References


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