SUMMARY We have assessed resting myocardial contractility and its baroreflex control in normotensive and hypertensive conscious rabbits. Hypertension was induced by bilateral cellophane wrapping of the kidneys with experiments performed 6 weeks later during the established phase of hypertension. The peak rate of change of left ventricular pressure (peak LV dP/dt) was used as the index of myocardial contractility. Baroreflex control of contractility and heart period (HP) was assessed by constructing stimulus response curves relating change in mean arterial pressure (MAP), induced by balloon occluders around the abdominal aorta and inferior vena cava, to change in peak LV dP/dt and HP. These stimulus response curves were obtained in normotensive rabbits with and without cardiac pacing, and in both normotensive and hypertensive animals after cardiac beta sympathetic blockade with propranolol, vagal blockade with methylscopolamine, and combined cardiac autonomic blockade with propranolol and scopolamine, as well as in rabbits with intact autonomic effectors.

Resting MAP was significantly higher in the hypertensive rabbits (119 ± 2 mm Hg) compared to normotensive controls (76 ± 1 mm Hg). Resting peak LV dP/dt was also greater by 51% in the hypertensive animals (7054 ± 287 mm Hg sec⁻¹) compared to controls (4690 ± 223 mm Hg sec⁻¹). There was no significant difference in the resting heart period or resting left ventricular end diastolic pressure. Transient changes in MAP induced by occlusion of the aortic or venous balloons produced significant alterations in peak LV dP/dt in normotensive animals with and without pacing and in hypertensive control animals. In animals with cardiac sympathetic block, the range and slope or sensitivity of the stimulus response curves were not significantly changed but in animals with vagal block pressure the sensitivity was reduced by 90% and the range at 30 mm Hg by 88%. After propranolol and methylscopolamine were administered together, the stimulus no longer evoked a response. These experiments demonstrate that myocardial contractility is under baroreflex control and suggest that this is mediated principally via parasympathetic nerves to the heart. There was no significant difference between the sensitivity of baroreflex control of myocardial contractility in the normotensive (−84 ± 14 mm Hg sec⁻¹ per mm Hg) and the hypertensive (−110 ± 14 mm Hg sec⁻¹ per mm Hg) rabbits, unlike the baroreflex control of heart period where sensitivity was markedly impaired in the hypertensive (sensitivity 3.8 ± 0.8 msec/mm Hg) compared to the normotensive (6.9 ± 1.0 msec/mm Hg) animals. (Hypertension 5: 916-926, 1983)

KEY WORDS  • left ventricular pressure  • mean arterial pressure  • cardiac pacing  • balloon occlusion  • parasympathetic nerves

Myocardial contractility has not been extensively studied in hypertension. Indeed there are no studies of myocardial contractility in the early stages of clinical human hypertension, and such evidence as there is in relation to experimental hypertension is conflicting.1,2 Whereas contractility has been reported to be increased early in the development of one-kidney Goldblatt hypertension in conscious dogs,2 it is thought to be decreased in established two-kidney Goldblatt hypertension in anesthetized rats.4

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Regulation of myocardial contractility by baroreceptor reflexes has not been studied in hypertension, although it has been investigated to a limited extent in normal animals. Baroreflexes have been demonstrated to influence myocardial contractility in normotensive anesthetized animals5–8, but the evidence is equivocal in conscious animals. Vatner et al.9 were unable to demonstrate reflex control of contractility after bilateral carotid occlusion or carotid sinus nerve stimulation, but more recent studies using balloon occluders around the inferior vena cava suggest that baroreflexes do influence the myocardial contractile state in unanesthetized animals.10 It is well established that arterial baroreflexes regulate heart rate in both normotensive and hypertensive preparations, and that the sensitivity of the baroreceptor heart rate reflex is decreased in both clinical and experimental hypertension.11–14

Most recent studies of baroreflex control of heart rate14,15 have used mathematically derived sigmoid
curves to describe the stimulus response relationship between mean arterial pressure (MAP) and heart period (HP), and alterations in baroreflex control are clearly reflected by changes in the parameters of the curve. We have therefore used an exponential curve to describe the stimulus response relationship between rises in MAP and changes in myocardial contractility, to help us describe and quantitate with greater accuracy the changes in baroreflex control of contractility.

We designed our present experiments to study the changes in resting myocardial contractility in animals with experimental renal hypertension and to compare baroreflex control of myocardial contractility in normotensive and hypertensive animals. We were particularly interested to see if the baroreceptor control of myocardial contractility in hypertension was impaired in the same way as has been reported for baroreceptor reflex control of heart rate.

**Methods**

**Operative Procedures**

Male and female rabbits of mixed breed (average body weight, 2.5 kg) were studied in the conscious state. All operative procedures were carried out under halothane anesthesia after induction with propranolol (Eptontol, Bayer, 30 mg/kg/i.v.). All intrathoracic procedures required assisted ventilation.

Balloon occluders were placed around the inferior vena cava through a right thoracic incision and around the abdominal aorta via a midline abdominal incision. In some animals, epicardial pacing electrodes were sewn on to the left atrium via a left thoracic incision. The animals were allowed to rest quietly in individual boxes before the experiment. Experiments were conducted 2 days later when the animals had completely recovered.

Renal hypertension was produced by cellophane wrapping of both kidneys through a retroperitoneal incision and further operative procedures were performed after recovery at least 1 week later. Experiments in hypertensive rabbits were performed 6 weeks later during the established phase of hypertension.

**Experimental Protocol**

On the day of the experiment, after local infiltration with lidocaine 0.5%, the central ear artery and marginal ear vein were cannulated, and the occluder tubing, pacing wires, and left ventricular pressure catheter were exteriorized. The animals were then allowed to rest quietly in individual boxes before the experiment was started.

Arterial pressure was measured with a Statham P23D pressure transducer (Statham Corporation, San Juan, Puerto Rico). The left ventricular pressure catheter was connected to a Millar catheter micromanometer (Millar Instruments, Inc., Houston, Texas) via a 17-gauge blunted needle. This fluid-filled catheter transducer system has a natural resonant frequency of 100 Hz and a damping coefficient of 0.6 and is suitable for recording a high fidelity left ventricular pressure (LVP) trace and its derivative LV dP/dt. Using a Philbrick operational amplifier (Teleadyne Philbrick, Dedham, Massachusetts) connected as a differentiator, we derived LV dP/dt from LVP, enabling us to measure peak LV dP/dt. A triangular wave with known slope (rate of change) was substituted for the pressure signal so as to give direct calibration of the dP/dt signal. Heart rate (HR) was recorded on a beat-to-beat basis by a cardiac tachometer triggered by the pressure pulse. Heart period (time between successive beats, in msec) was measured from the left ventricular pressure trace.

Continuous records of phasic and mean arterial pressure (MAP), LV, high gain LVP, LV dP/dt, and HR were displayed on an 8 channel Gould 2800 biomedical recording system (Gould Inc., Instruments Division, Cleveland, Ohio), as shown in figure 1.

**Assessment of Baroreflex Control of Heart Period and Myocardial Contractility**

Rises and falls in arterial pressure were produced by eight pairs of graded inflations of the inferior vena cava and aortic balloon occluders at 5-minute intervals. Changes in heart period and peak LV dP/dt were measured at steady state 10-15 seconds later. In some animals, heart rate was held constant just above the resting heart rate by atrial pacing.

The characteristics of the baroreceptor heart period reflex for each individual rabbit were obtained by fitting the observed values of MAP and heart period (HP) to the logistic function:

$$HP = a + \left[ \frac{b}{1 + e^{c(MAP - d)}} \right],$$

using nonlinear least-squares regression analysis. The parameters of this function represent the lower plateau of the sigmoid curve (a), the heart period range (b), the MAP at the midpoint of the range (d), and the slope or sensitivity of the curve at this point (−bc/4), as described by West et al. (fig. 2 left). To obtain the average curve for a group of rabbits, the mean of each parameter was calculated and these values were then substituted into the logistic function above, to generate the stimulus response curves.

The reflex effects of changes in MAP on peak LV dP/dt were assessed in two ways. Inflation of the aortic balloon had little direct mechanical effect on LV dP/dt despite the increase in afterload, in agreement with the findings of Mahler et al. and it was possible to construct stimulus response curves using increases in arterial pressure ranging from 2 to 30 mm Hg. The characteristics of the reflex change in peak LV dP/dt following aortic balloon inflation were defined for each individual rabbit by fitting the observed data for the change in MAP (ΔMAP) and the change in con
tractility (ΔC) to the exponential function $ΔC = a(1 - e^{-bΔMAP})$ by nonlinear least-squares regression analysis. The parameters of this function represent the plateau of the exponential curve (a) and the slope or sensitivity of the response (ab) at mean resting MAP and mean resting peak LV dP/dt for each individual rabbit (fig. 2 right).

The average stimulus response curve for each group of rabbits was obtained by calculating the mean of each parameter and substituting the values obtained into the exponential function above (fig. 3). The extent of the response to a rise in MAP of 30 mm Hg, corresponding to the maximum stimulus applied, has been termed the "Range" (R30) and was derived from the regression equation as illustrated in figure 2b right.

Reflex changes in LV dP/dt produced by occlusion of the venous balloon were opposed by profound direct effects resulting from changes in preload, so that it was not possible to construct stimulus response curves. However, a qualitative analysis of the reflex effects was obtained by comparing the changes in peak LV dP/dt after small falls in arterial pressure of the order of 4–6 mm Hg with those seen after larger reductions around 16–26 mm Hg. With the smaller falls in arterial pressure produced by slight occlusion of the venous balloon, the depressant effect of changes in preload was insufficient to mask the reflex rise in LV dP/dt completely. With larger falls in pressure produced by more vigorous occlusion of the venous balloon, the decrease in dP/dt caused by the reduction in preload was of sufficient magnitude to mask the reflex increase altogether. Changes in peak LV dP/dt were determined for each individual rabbit and then averaged to give values for each experimental group.

**Drug Administration**

Cardiac beta sympathetic blockade was produced by the administration of propranolol (initial dose of 500 μg/kg i.v. followed by 100 μg/min i.v.). Cardiac vagal blockade was produced by the administration of methylscopolamine (initial doses of 50 μg/kg i.v., supplemented by 25 μg/kg every 30 minutes). Combined blockade of cardiac sympathetic and vagal effectors was produced by the administration of the two drugs together.

**Statistical Methods**

The significance of changes in the different circulatory variables and in the parameters of stimulus response curves of various groups was assessed by anal-
Figure 2. Left: Mean arterial pressure (MAP)-heart period (HP) stimulus response curve in a single animal. Points represent the observed data at the steady state following lowering and raising of MAP by inflation of balloon occluders. The curve is obtained by fitting the data points to the equation shown, using nonlinear least-squares regression analysis. $a =$ position of the lower plateau; $b =$ the range between upper and lower plateau; $-bc/4 =$ slope or sensitivity at midrange of the blood pressure, $d$. Right: MAP-myocardial contractility relationship in a single animal. Points represent the observed data at a steady state following elevation of MAP by inflation of the aortic balloon. The curve is obtained by fitting the observed data for change ($\Delta C$) in peak LV $dP/dt$ and corresponding rise ($\Delta MAP$) in MAP to the equation shown using nonlinear least squares regression analysis. This gives for each animal the parameters $ab$, the slope or sensitivity at resting MAP and contractility, and the plateau value of the curve, $a$. The "range" at $MAP$ of 30 mm Hg ($R_{30}$) is obtained from the fitted curve.

Results

Resting Hemodynamic Parameters in Normotensive and Hypertensive Rabbits

Mean arterial pressure was increased by 57% in rabbits with renal hypertension produced by bilateral wrapping with cellophane (119 ± 2 mm Hg) compared to normotensive controls (76 ± 1 mm Hg; $p < 0.01$; table 1). The resting peak LV $dP/dt$ in the absence of cardiac blocking drugs was also 51% greater in the hypertensive animals ($p < 0.01$; table 1). There was no significant difference in either the heart period or the left ventricular end diastolic pressure (LVEDP) between the normotensive and hypertensive rabbits (table 1).

Administration of propranolol did not significantly affect MAP, LVEDP, or peak LV $dP/dt$ in either group of animals. The heart period increased after propranolol administration and decreased after methylscopolamine administration in both normotensive and hypertensive rabbits; it was not significantly different from control values when the two drugs were given together (table 1).

Stimulus Response Curves Relating Peak LV $dP/dt$ to MAP in Normotensive Rabbits

Inflation of the Aortic Balloon

Inflation of the aortic balloon caused a rise in arterial pressure with a reflex increase in HP and decrease in peak LV $dP/dt$ (figs. 1 and 2). The stimulus response curves relating the fall in peak LV $dP/dt$ to the rise in MAP in the different groups of rabbits are shown in figure 3. The sensitivity of the baroreceptor-contraction reflex is greatest with small changes in pressure, as is the case with the baroreceptor-heart period reflex and the baroreceptor-peripheral blood flow reflex, so that the initial part of the stimulus response curve is the steepest, tending toward a plateau for greater changes in pressure (fig. 3 left).
### Table 1. Resting Mean MAP, HP, LVEDP, and Peak LV dP/dt

<table>
<thead>
<tr>
<th>Rabbit group</th>
<th>No.</th>
<th>MAP (mm Hg)</th>
<th>HP (msec)</th>
<th>LVEDP (mm Hg)</th>
<th>Peak LV dP/dt (mm Hg sec⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normotensive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>8</td>
<td>76 ± 1</td>
<td>242 ± 8</td>
<td>4.8 ± 0.3</td>
<td>4690 ± 223</td>
</tr>
<tr>
<td>Propranolol</td>
<td>5</td>
<td>81 ± 1</td>
<td>279 ± 8*</td>
<td>6.0 ± 0.3</td>
<td>4728 ± 223</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>6</td>
<td>79 ± 1</td>
<td>203 ± 8*</td>
<td>4.5 ± 0.3</td>
<td>4876 ± 223</td>
</tr>
<tr>
<td>Propranolol + scopolamine</td>
<td>6</td>
<td>79 ± 1</td>
<td>241 ± 8</td>
<td>5.0 ± 0.3</td>
<td>3947 ± 223</td>
</tr>
<tr>
<td><strong>Hypertensive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>8</td>
<td>119 ± 2†</td>
<td>238 ± 6</td>
<td>3.9 ± 0.5</td>
<td>7054 ± 287‡</td>
</tr>
<tr>
<td>Propranolol</td>
<td>6</td>
<td>117 ± 2†</td>
<td>292 ± 6*</td>
<td>5.9 ± 0.5</td>
<td>5469 ± 287†</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>4</td>
<td>123 ± 2†</td>
<td>213 ± 6*</td>
<td>3.7 ± 0.5</td>
<td>6658 ± 287‡</td>
</tr>
<tr>
<td>Propranolol + scopolamine</td>
<td>7</td>
<td>119 ± 2†</td>
<td>251 ± 6</td>
<td>4.1 ± 0.5</td>
<td>5693 ± 287‡</td>
</tr>
</tbody>
</table>

Values are means ± SEM derived from analysis of variance.
* p < 0.05, compared with control animals within the normotensive and hypertensive groups.
† p < 0.01, compared with control animals within the normotensive and hypertensive groups.
‡ p < 0.01, compared with corresponding groups of normotensive and hypertensive rabbits.

**Figure 3.** Average MAP-myocardial contractility stimulus response curves for normotensive and hypertensive rabbits. The effects of beta-sympathetic blockade with propranolol, vagal blockade with methylscopolamine, and combined blockade with both propranolol and scopolamine are shown. Statistical analysis of the data shown in these curves is given in Table 2 and Figure 4.
TABLE 2. Sensitivity and Range of Stimulus Response Curves Relating Change in Contractility to Change in MAP

<table>
<thead>
<tr>
<th>Rabbit group</th>
<th>No.</th>
<th>Sensitivity (mm Hg sec⁻¹/mm Hg)</th>
<th>R₃₀ (Range at 30 mm Hg rise in MAP) (mm Hg sec⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>8</td>
<td>-84 ± 14</td>
<td>-1248 ± 92</td>
</tr>
<tr>
<td>Propranolol</td>
<td>5</td>
<td>-39 ± 14</td>
<td>-802 ± 92</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>6</td>
<td>-9 ± 14†</td>
<td>-147 ± 92†</td>
</tr>
<tr>
<td>Propranolol + scopolamine</td>
<td>6</td>
<td>+8 ± 14†</td>
<td>+134 ± 92†</td>
</tr>
<tr>
<td>Hypertensive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>8</td>
<td>-110 ± 14</td>
<td>-1402 ± 167</td>
</tr>
<tr>
<td>Propranolol</td>
<td>6</td>
<td>-39 ± 14*</td>
<td>-696 ± 167</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>4</td>
<td>-33 ± 14†</td>
<td>-297 ± 167†</td>
</tr>
<tr>
<td>Propranolol + scopolamine</td>
<td>7</td>
<td>-2 ± 14†</td>
<td>-39 ± 167†</td>
</tr>
</tbody>
</table>

Values are means ± SEM derived from analysis of variance.
* p < 0.05, compared with control animals within the normotensive and hypertensive groups.
† p < 0.01, compared with control animals within the normotensive and hypertensive groups.

Cardiac beta sympathetic blockade produced by the administration of propranolol caused a slight reduction in both the sensitivity and the range (R₃₀) of the baroreceptor-contractility curve, but these changes were not significant (fig. 3, left, fig. 4, and table 2). On the other hand, vagal blockade produced by the administration of methylscopolamine almost abolished the reflex fall in LV dP/dt (fig. 3) and reduced the sensitivity and range (R₃₀) by 88-90% (fig. 4 and table 2). Combined blockade of cardiac vagal and beta sympathetic effectors produced by administration of both propranolol and methylscopolamine completely abolished the fall in LV dP/dt seen after inflation of the aortic balloon.

Inflation of Aortic Balloon in Paced Animals

In paced animals with the heart rate held constant just above resting levels, inflation of the aortic balloon still caused a decrease in peak LV dP/dt even though the bradycardia was prevented (figs. 1 and 5; table 3). The magnitude of the decrease in LV dP/dt (range at 30 mm Hg), was reduced by one-third after pacing in intact animals not receiving any autonomic blocking drugs (fig. 5 and table 3). When the same animals were given propranolol and scopolamine, the fall in LV dP/dt produced by aortic balloon inflation was completely abolished (fig. 5 and table 3) and in fact reversed.

Inflation of the Venous Balloon

Inflation of the venous balloon caused a reflex decrease in HP and a variable change in peak LV dP/dt depending upon the magnitude of the change in pressure (fig. 6; table 4). Thus, with small changes in MAP in unblocked control animals, there was a small rise in peak LV dP/dt (fig. 6; table 4). With larger decreases in MAP of the order of 16–26 mm Hg, induced by more vigorous inflation of the venous balloon, there was a drop in peak LV dP/dt (fig. 6 and table 4).

With both small and large decreases in MAP (4–6 and 16–26 mm Hg respectively), the changes in peak LV dP/dt were similar in control animals and in animals treated with propranolol (fig. 6; table 4). In animals treated with methylscopolamine, however, the small rise in LV dP/dt seen in control animals with 4–6 mm Hg changes in MAP was reversed so that LV dP/dt actually fell (fig. 6; table 4). With larger decreases in MAP (16–26 mm Hg), the drop in LV dP/dt was accentuated (fig. 6). Combined administration of pro-
RISE IN MAP (mmHg)

CHANGE PEAK LV dP/dt (mmHg/sec)

FIGURE 5. Average MAP-myocardial contractility stimulus response curves for normotensive rabbits when the heart rate was allowed to change, or was held constant by atrial pacing, or was held constant by atrial pacing and both beta-adrenoceptors and vagal receptors were blocked by propranolol and scopolamine. Statistical analysis of these data is given in table 3.

TABLE 3. Sensitivity and Range of Stimulus Response Curves Relating Change in Contractility to Change in MAP in Paced Animals

<table>
<thead>
<tr>
<th>Normotensive group</th>
<th>No.</th>
<th>Sensitivity (mm Hg sec⁻¹ per mm Hg)</th>
<th>R₃₀ (mm Hg sec⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>7</td>
<td>-133 ± 26</td>
<td>-158 ± 158 *</td>
</tr>
<tr>
<td>Paced</td>
<td>7</td>
<td>-58 ± 26</td>
<td>-1036 ± 158 *</td>
</tr>
<tr>
<td>Paced + propranolol + scopolamine</td>
<td>7</td>
<td>+8 ± 26†</td>
<td>+412 ± 158 ††</td>
</tr>
</tbody>
</table>

Values are means ± SEM derived from analysis of variance.

* p < 0.05, compared with unpaced control animals.
† p < 0.01, compared with unpaced control animals.
‡ p < 0.05, compared with paced animals without autonomic blockade.

Table 3 shows the sensitivity and range of stimulus response curves relating change in contractility to change in MAP in paced animals. Propranolol and methylscopolamine also reversed the small increase in peak LV dP/dt produced by small inflations of the venous balloon in control animals and markedly accentuated the decrease seen with large inflations (fig. 6; table 4).

Stimulus Response Curves Relating Peak LV dP/dt to MAP in Hypertensive Rabbits

Inflation of the Aortic Balloon

The rise in MAP in hypertensive rabbits with intact effector mechanisms was again accompanied by a reflex increase in HP (fig. 7) and decrease in peak LV dP/dt (fig. 3 right). The sensitivity and range of the stimulus response curves relating the change in MAP to the change in peak LV dP/dt are shown in figure 4 and table 2, and were very similar to those seen in normotensive rabbits. The changes in the stimulus response curves produced by propranolol alone, methylscopolamine alone, or by the two drugs together, were very similar to those observed in normotensive rabbits (figs. 3 and 4; table 2).

Inflation of the Venous Balloon

The effects of venous balloon inflation on peak LV dP/dt in hypertensive animals with intact autonomic effectors were similar to those seen in normotensive animals (fig. 6). With small decreases in MAP produced by inflation of the venous balloon, the effects of propranolol, of methylscopolamine, or of both drugs together in these hypertensive rabbits were similar to those seen in corresponding groups of normotensive rabbits (fig. 6; table 4). With the larger drops in MAP produced by more vigorous inflation of the venous balloon, the effects of autonomic blockade were also qualitatively similar in the hypertensive and normotensive groups (fig. 6; table 4).

Comparison of Arterial Pressure-Heart Period Curves in Normotensive and Hypertensive Rabbits

Baroreflex-heart period curves were constructed for both normotensive and hypertensive rabbits (fig. 7 top) and the parameters describing these curves are shown in table 5. The curve for the hypertensive rabbits was shifted to the right, reflecting the increase in pressure, with a 41 mm Hg rise in MAP at midrange. The curve was also clearly flatter (fig. 7 top), reflecting the lower sensitivity of the reflex (table 5).

Discussion

Changes in Resting Myocardial Contractility

Both resting MAP and resting peak LV dP/dt were increased by approximately 50% in animals with established hypertension produced by bilateral wrapping of the kidneys with cellophane (table 1). While there are a number of indices of myocardial contractility, peak LV dP/dt is generally accepted to be an isovolumic index of contractility and to be relatively independent of afterload, particularly in the presence of high aortic diastolic pressures. Since peak LV dP/dt is principally determined by the inotropic state.
the increase in peak LV dP/dt observed in the hypertensive animals probably reflects a rise in myocardial contractility. Although peak LV dP/dt can be influenced by the heart rate,24,26 this factor was not operative in the present study since the resting heart rate was similar in normotensive and hypertensive rabbits (table 1). The left ventricular end diastolic pressure was also similar in the hypertensive and normotensive rabbits (table 1), and well within the normal range so that changes in preload were unlikely to be responsible for the increase in LV dP/dt. Furthermore, Broughton and Korner24 have demonstrated that increases in preload over the full width of the normal range could only produce changes of the order of 15% in peak LV dP/dt. It seems likely, therefore, that the 51% increase in peak LV dP/dt found in our hypertensive rabbits reflects a real and significant increase in myocardial contractility. A comparable rise of 61% was reported in myocardial contractility in conscious dogs with unilateral Goldblatt hypertension using the index LV dP/dt at 40 mm Hg.3

Since the cardiac output is known to be depressed 6 weeks after bilateral wrapping of the kidneys,27 it seems that the increase in peak LV dP/dt represents a

**TABLE 4.** Change in Peak LV dP/dt Following Venous Balloon Inflation

<table>
<thead>
<tr>
<th>Rabbit group</th>
<th>No.</th>
<th>4-6 mm Hg fall in MAP</th>
<th>16-26 mm Hg fall in MAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive Control</td>
<td>5</td>
<td>+ 241 ± 76</td>
<td>- 584 ± 226</td>
</tr>
<tr>
<td>Propranolol</td>
<td>5</td>
<td>+ 280 ± 76</td>
<td>- 551 ± 226</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>5</td>
<td>- 226 ± 76</td>
<td>- 800 ± 226</td>
</tr>
<tr>
<td>Propranolol + scopolamine</td>
<td>5</td>
<td>- 125 ± 76</td>
<td>- 1142 ± 226</td>
</tr>
<tr>
<td>Hypertensive Control</td>
<td>5</td>
<td>+ 510 ± 163</td>
<td>- 452 ± 170</td>
</tr>
<tr>
<td>Propranolol</td>
<td>5</td>
<td>+ 332 ± 163</td>
<td>- 306 ± 170</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>4</td>
<td>+ 127 ± 163</td>
<td>- 957 ± 170</td>
</tr>
<tr>
<td>Propranolol + scopolamine</td>
<td>5</td>
<td>- 111 ± 163</td>
<td>- 548 ± 170</td>
</tr>
</tbody>
</table>

Values are means ± SEM derived from analysis of variance. *p < 0.05, compared with control animals within the normotensive or hypertensive groups. t p < 0.01, compared with control animals within the normotensive or hypertensive groups.
secondary or compensatory change in the face of increasing blood pressure and increasing afterload, rather than a major element in the pathogenesis of the elevated pressure. It should be noted that the increase in peak LV dP/dt is occurring at 6 weeks, a time at which left ventricular hypertrophy is well documented in this model. While there is clear evidence that ventricular hypertrophy is associated with a decrease in the contractile state of the ventricular muscle, it is possible that an increase in ventricular mass could contribute to an increase in total contractile force of the intact ventricle and be reflected in our measurements of peak LV dP/dt.

Cardiac vagal blockade did not alter resting arterial pressure or peak LV dP/dt in either normotensive or hypertensive animals (table 1). Beta-adrenoceptor blockade also failed to alter blood pressure in both sets of animals, but whereas it caused a 22% decrease in peak LV dP/dt in the hypertensive animals, it did not lower peak LV dP/dt in normotensive rabbits (table 1). This raises the possibility that the increase in peak LV dP/dt in the hypertensive rabbits at rest is mediated at least partly through an increase in resting sympathetic activity. Since beta adrenoceptor block did not restore the LV dP/dt of hypertensive rabbits to the levels observed in normotensive animals (table 1), it seems likely that other factors, either structural or humoral, also contribute to the increase in resting myocardial contractility.

Baroreflex Control of Myocardial Contractility in Normotensive Rabbits

Inflation of balloon occluders produces changes in the hemodynamic variables as a result of direct mechanical effects, as well as of reflex effects mediated, in part, through arterial baroreceptor reflexes. The resultant changes in peak LV dP/dt therefore represent the balance or sum of direct mechanical and reflex effects. While these studies were designed to investigate the role of arterial baroreceptor reflexes, they do not exclude contributions from other cardiopulmonary reflexes to some of the responses observed.

The present experiments clearly demonstrate that myocardial contractility is under baroreceptor reflex control in conscious rabbits. Elevation of MAP following inflation of the aortic balloon produced a substantial drop in peak LV dP/dt, which was completely abolished by combined cardiac blockade (fig. 3). It should be noted that, in the presence of cardiac blockade produced by propranolol plus methylscopolamine, the response observed after balloon inflation reflects purely mechanical events since the baroreflex efferents to the heart are inactivated. Thus, the fall in peak LV dP/dt seen in animals without autonomic block must be the result of reflex changes mediated through cardiac vagal and sympathetic efferent mechanisms, and cannot be attributed to the direct mechanical effects of a rise in afterload. While the reflex fall in heart rate contributes approximately one-third to the decrease in peak LV dP/dt after aortic balloon inflation in un paced animals, it cannot account for the remaining two-thirds of the decrease, which was still evident in animals with

<table>
<thead>
<tr>
<th>Rabbit group</th>
<th>MAP at midrange (mm Hg)</th>
<th>Sensitivity (ms/min Hg)</th>
<th>Heart period range (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive</td>
<td>82.6 ± 2.5</td>
<td>6.9 ± 1.1</td>
<td>145.8 ± 12.6</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>126.7 ± 4.7*</td>
<td>3.8 ± 0.8*</td>
<td>147.6 ± 20.0</td>
</tr>
</tbody>
</table>

Values are means ± SEM.

*p < 0.05, compared with normotensive rabbits.
constant heart rate (fig. 5 and table 3), in agreement with Yoran et al.10

The reflex fall in peak LV dP/dt after aortic balloon inflation is predominantly mediated through the vagus nerve (figs. 3 and 4). Beta-adrenergic receptor blockade did not significantly alter the arterial pressure-contractility curves shown in figure 3, whereas vagal blockade almost completely abolished the fall in contractility. Thus, after methylscopolamine, the sensitivity of the reflex is reduced to 10% of control values while the range at 30 mm Hg is reduced to 12% of normal (table 2). It seems likely that the cardiac sympathetic nerves do make a small contribution to baroreflex control of contractility since the administration of propranolol produces similar shifts in the stimulus response curves when given to intact animals or to animals with vagal blockade (fig. 3).

Following inflation of the venous balloon, the reflex changes in peak LV dP/dt were opposed by direct mechanical effects on preload. As a result, an increase in LV dP/dt could only be seen with small decreases in arterial pressure, and any reflex tendency to raise the LV dP/dt was completely masked with larger falls in pressure (table 4 and fig. 6). The reflex changes are once again predominantly mediated through the vagus (fig. 6).

**Baroreflex Control of Myocardial Contractility in Hypertensive Rabbits**

The stimulus response curves relating changes in peak LV dP/dt to changes in mean arterial pressure following aortic balloon inflation were very similar in hypertensive animals and in normotensive rabbits (figs. 3 and 4; table 2). The pattern of changes in peak LV dP/dt evoked by decreased arterial pressure as a result of vena caval balloon inflation was also similar in conscious hypertensive and normotensive animals (fig. 6). These results demonstrate that myocardial performance in animals with chronic renal hypertension is under reflex baroreceptor control and that this control is predominantly mediated through the vagus.

As previously reported,11-14 baroreflex control of heart rate is blunted in the hypertensive animals, as manifest in a reduced sensitivity of the baroreceptor-heart period curve (table 5; fig. 7). On the other hand, baroreflex control of myocardial contractility does not appear to be impaired in this way, and the sensitivity and range of the arterial pressure-contractility curves are similar in the hypertensive and normotensive animals (table 2; fig. 4). As can be seen from figure 7, the arterial pressure-contractility curve obtained with aortic balloon inflation was merely shifted as a result of the increase in pressure and in contractility; the parameters describing the curve were not affected (table 2). This finding is consistent with the report of Guo et al.31 that baroreflex control of hindlimb vascular resistance was preserved following denervation of carotid or aortic baroreceptors despite impaired heart-rate control. These results raise the possibility that either the afferent or the central mechanisms responsible for baroreceptor control of contractility may differ from those involved in the regulation of heart rate.

**References**


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Baroreflex control of myocardial contractility in conscious normotensive and renal hypertensive rabbits.

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