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Intrarenal Blood Flow in Dogs with Normal and Spontaneously Elevated Blood Pressure[1] (39600)

ROBERT O. BANKS

Department of Physiology, University of Cincinnati, College of Medicine, Cincinnati, Ohio 45267

A large number of physiological and pharmacological stimuli alter the distribution of blood flow within the kidney. Recently, Abe *et al.* (1) investigated the influence of blood pressure per se on the distribution of blood flow within the kidney. In these studies, renal perfusion pressure was varied by means of aortic clamping. No effects on intrarenal distribution were detected when renal perfusion pressure was decreased from control values (142 ± 5 mm Hg) to 105 mm Hg. In contrast, reduction of pressure below 100 mm Hg increased inner cortical flow and decreased outer cortical flow.

At the present time, no information is available concerning the distribution of blood flow within the kidney as a function of the spontaneously occurring blood pressure. Therefore, we studied the distribution of intrarenal blood flow utilizing radiolabeled microspheres in 60 nondiuretic, pentobarbital-anesthetized mongrel dogs as a function of their spontaneous mean arterial blood pressure. These studies are of interest in view of our previous report that bilateral carotid occlusion with the resultant increase in renal perfusion pressure results in selective increases in inner cortical vascular resistance (2).

Methods. Sixty mongrel dogs of either sex (10–15 kg) were anesthetized with pentobarbital (30 mg/kg iv). The animals were tracheotomized, and positive pressure ventilation was applied with a Harvard Apparatus large animal respirator. A solution containing *para*-aminohippurate (PAH) and creatinine in saline was administered iv at 0.2 ml/min/kg body wt via a PE-100 catheter inserted into the right external jugular vein. Blood pressure was recorded with a Physiograph pressure transducer (P-1000A) and recorder (Four-A) via a PE-100 catheter inserted into the right femoral artery. The left femoral artery was also cannulated with a PE-100 catheter, and the catheter tip was advanced into the thoracic aorta several inches above the renal arteries. This left femoral artery catheter served for collection of arterial blood samples and injection of microspheres (see below for details). Renal venous samples were obtained through Kifa catheters (U.S. Catheter Corp.) positioned in the right and left renal veins via the femoral veins. Right and left ureters were cannulated with PE-100 tubing.

When urine flow had stablized (1.5 to 2.5 hr), two consecutive clearance periods were performed with midpoint arterial and renal venous samples. Approximately 200,000 ^{169}Yb-labeled microspheres (15 ± 5 μm; 3M Corp.) were then rapidly injected into the thoracic aorta. A number of different experimental manipulations followed these control estimates of blood flow distribution, but the results are not germain to the current report. At the termination of each experiment both kidneys were removed, weighed, and placed in 10% formaldehyde solution overnight. Saggital kidney sections (approx 0.5 cm) were then manually cut. Two cortical zones, approximately equal in thickness, were easily discernible: a dark outer cortex and a light inner cortex. With the exception of the superior and inferior renal poles, the entire outer cortex was then removed, weighed, and radioactivity was determined. Any outer cortex remaining on the renal pieces was removed, and the entire inner cortex was dissected free, weighed, and counted. Total microsphere content in each kidney was calculated from the sum of outer and inner cortical counts plus the counts of residual material. Radioactivity was determined on a Packard gamma scintillation counter (Model 3002).

Creatinine concentration was estimated

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by the picric acid method of Folin and Wu (6), and PAH by the diazotization procedure of Bratton and Marshall (4). Na^+ and K^+ concentrations were measured with flame photometry (Advanced Instruments Corp.).

Renal blood flow (RBF) was calculated from PAH clearance, renal extraction of PAH, and hematocrit values. Blood flow per gram outer (f_{oc}) or inner (f_{ic}) cortex was calculated according to the method of Katz *et al.* (8).

Data shown in each figure and table represent means and standard errors. However, the reported linear regression equations were derived from individual data points rather than the means.

Results. The mean blood pressures of the 60 anesthetized dogs reported in this study ranged from 90 to 180 mm Hg. The number of dogs at each mean arterial blood pressure and corresponding RBF, total renal resistance (R_T) and glomerular filtration rate (GFR) values are summarized in Table I. Renal resistance is expressed as peripheral resistance units per gram kidney weight. The dogs were characterized by a poor but nonetheless significant inverse relationship between RBF per gram kidney weight and mean arterial blood pressure. The linear regression equation for RBF and blood pressure was: $RBF = 0.015\ \overline{BP} + 6.64$ ($r = -0.239$, $P < 0.01$). Furthermore, evaluation of the relationship between total renal resistance and mean arterial blood pressure also revealed a significant correlation. The least squares line was $R_T = 0.30\ \overline{BP} - 9.32$ ($r = 0.464$, $P < 0.001$). Glomerular filtration rate did not significantly correlate with arterial blood pressure ($GFR = 0.0013\ \overline{BP} + 0.44$, $r = 0.162$, $P < 0.1$). As may be seen in Table I, the average GFR for the 60 dogs was 0.62 ml/min/g kidney wt ± 0.02 (SE).

Intrarenal blood flow distribution in the 60 dogs is shown in Fig. 1, a plot of inner and outer cortical blood flow per gram tissue vs mean arterial blood pressure. Outer cortical flow (f_{oc}) did not significantly correlate with blood pressure ($r = 0.12$, $P > 0.1$). In sharp contrast, inner cortical flow (f_{ic}) decreased significantly as mean arterial pressure increased ($r = -0.534$, $P < 0.001$). It is also important to note that over the spontaneous blood pressure range of 140–110 mm Hg (see Discussion for significance of this pressure range), there was also a significant relationship between mean arterial blood pressure and inner cortical flow ($f_{ic} = -0.06\ \overline{BP} + 12.41$, $r = -0.442$, $P < 0.001$). Thus, lower renal blood flows in dogs with elevated blood pressures was largely due to lower inner cortical blood flow values.

As would be predicted from the above data, regional resistance also increased with mean systemic pressure. In Fig. 2, inner (R_{ic}) and outer (R_{oc}) cortical resistance, calculated from blood flow per gram inner or outer cortex and mean systemic pressure, is plotted as a function of blood pressure. Both R_{ic} and R_{oc} significantly correlated with mean arterial blood pressure. It should be noted that the slope of R_{ic} vs $\overline{BP}$ was nearly an order of magnitude greater than that found with R_{oc} vs $\overline{BP}$.

TABLE I. MEAN ARTERIAL BLOOD PRESSURES, RENAL BLOOD FLOWS, GLOMERULAR FILTRATE RATES, AND RENAL VASCULAR RESISTANCE IN ANESTHETIZED DOGS.[a]

Number of dogs	Arterial mean blood pressure	RBF (ml/min/g kidney wt)	GFR (ml/min/g kidney wt)	R_T (mm Hg/ml/min/g)
3	90	5.4 ± 0.5	0.54 ± 0.09	17.2 ± 1.4
4	110	5.0 ± 0.2	0.67 ± 0.05	22.3 ± 0.6
9	120	4.8 ± 0.3	0.58 ± 0.04	27.6 ± 2.1
10	130	4.7 ± 0.2	0.58 ± 0.03	28.7 ± 1.2
11	140	4.5 ± 0.4	0.65 ± 0.04	36.3 ± 3.8
11	150	5.3 ± 0.3	0.67 ± 0.03	30.9 ± 1.9
10	160	4.4 ± 0.3	0.60 ± 0.04	40.5 ± 3.4
2	180	4.1 ± 0.1	0.77 ± 0.04	44.6 ± 1.3
$\bar{X}$	137 ± 20		0.62 ± 0.02	

[a] Values are means ± SE.

The wide range of intrarenal blood flow distribution noted above should have optimized evaluation of the potential involvement of this physiological parameter in the control of electrolyte excretion. Amounts of Na^+ ($U_{Na}V$) and K^+ (U_KV) excreted per gram kidney weight as well as fractional excretion of Na^+ (FE_{Na^+}) and K^+ (FE_{K^+}) are shown in Table II. Neither fractional nor absolute Na^+ excretion per gram kidney weight showed significant correlations with inner cortical flow, outer cortical flow, or with the ratio of inner to outer cortical blood flow (IC/OC). Indeed, $U_{Na}V$ per gram kidney weight was essentially constant, averaging 1.95 μEq/min/g kidney wt ± 0.78 (SE). In contrast, U_KV (microequivalents per minute per gram kidney weight) showed a poor but significant inverse correlation with the ratio of inner to outer cortical blood flow ratio ($U_KV = 0.27$ IC/OC + 0.66, $r = -0.24$, $P < 0.01$). However, this correlation between absolute potassium excretion and flow distribution may be fortuitous since FE_{K^+} and the IC/OC ratio were not significantly correlated.

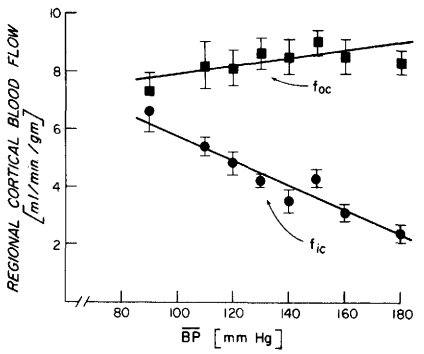

FIG. 1. Inner (f_{ic}) and outer (f_{oc}) cortical blood flow per gram inner or outer cortex (± SE) is shown as a function of mean arterial blood pressure. Linear regression lines are indicated ($f_{ic} = -0.04\ \overline{BP} + 9.99$, $r = -0.534$, $P < 0.001$; and $f_{oc} = 0.12\ \overline{BP} + 6.55$, $r = 0.12$, $P > 0.1$).

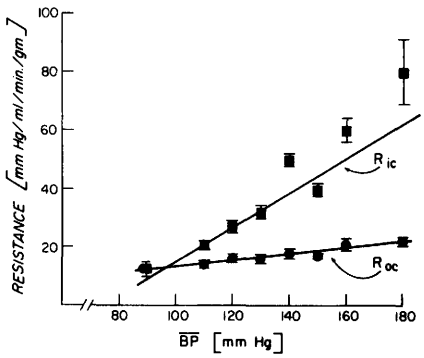

FIG. 2. Calculated values for inner (R_{ic}) and outer (R_{oc}) cortical resistance (± SE) are shown as function of blood pressure. Linear regression equations ($R_{ic} = 0.70\ \overline{BP} - 54.96$, $r = 0.64$; $P < 0.001$; and $R_{oc} = 0.10\ \overline{BP} + 3.14$, $r = 0.34$, $P < 0.001$) are drawn.

Discussion. The renal hemodynamic changes associated with hypertensive disorders are generally characterized by a decrease in renal blood flow and an increase in renal vascular resistance (3, 5, 7). The results obtained in this study show a similar inverse correlation between mean arterial blood pressure and total renal blood flow (Table I). Furthermore, calculated values for renal vascular resistance were approximately 2.5 times greater in those dogs at 180 mm Hg vs those at 90 mm Hg blood pressure (Table I).

As may be seen in Fig. 1, the distribution of intrarenal blood flow changed considerably as a function of mean arterial blood pressure. These changes in intrarenal blood flow were largely ascribable to differences in

TABLE II. Na^+ AND K^+ EXCRETION AT DIFFERENT BLOOD PRESSURES.[a]

Mean arterial blood pressure (mm Hg)	$U_{Na}V$ (μEq/min/g kidney wt)	U_KV	FE_{Na} %	FE_K %
90	0.6 ± 0.4	0.33 ± 0.05	0.5 ± 0.30	17 ± 4
110	1.9 ± 0.7	0.46 ± 0.07	1.9 ± 0.60	20 ± 2
120	1.4 ± 0.3	0.52 ± 0.04	1.8 ± 0.30	29 ± 2
130	1.9 ± 0.4	0.51 ± 0.04	2.4 ± 0.60	29 ± 2
140	2.1 ± 0.5	0.62 ± 0.07	2.7 ± 0.90	29 ± 2
150	2.8 ± 0.6	0.53 ± 0.04	3.1 ± 0.80	26 ± 3
160	1.8 ± 0.5	0.48 ± 0.04	2.3 ± 0.70	23 ± 2
180	1.4 ± 0.2	0.64 ± 0.06	1.2 ± 0.01	24 ± 3

[a] Values are means ± SE.

inner cortical hemodynamics. Thus, dogs with mean arterial pressures of 180 mm Hg were characterized by inner cortical blood flows which were approximately 1/3 that found in dogs with mean arterial pressures of 90 mm Hg. In addition, regional vascular resistance (Fig. 2) was significantly higher in the inner cortex compared to the outer cortex at elevated blood pressures.

The changes in intrarenal hemodynamics which were observed in the current study could be related to differences in myogenic, hormonal, or neurogenic factors in the inner cortex compared to the outer cortex. However, the results of Abe *et al.* (1) appear to rule out a myogenic factor since they have shown that changes in renal perfusion pressure alone between approximately 140 and 105 mm Hg did not influence intrarenal blood flow distribution. Renal perfusion pressure in their studies was controlled by means of aortic clamping. As was noted in the Results, we found a significant inverse correlation between inner cortical flow and mean arterial blood pressure in the 140- to 110-mm Hg range.

With respect to the other possibilities, i.e., hormonal or neurogenic factors, further experiments will be required to elucidate which variable accounts for the intrarenal hemodynamic events described in this study. Nonetheless, it is of interest to note that the current results are similar to the changes in intrarenal blood flow distribution which occur with bilateral carotid occlusion (2), a maneuver known to increase renal sympathetic nerve tone (9).

Finally, while it seems reasonable to assume that some parameter of renal function would be related to intrarenal flow distribution and that the substantial flow distribution differences we observed in these studies would have optimized elucidation of this function, no differences, at least with respect to Na^+ and K^+ excretion, were found (Table II). The possibility exists that other parameters of renal function are dependent on intrarenal flow distribution or that the functional changes are relatively small and cannot be detected during acute studies.

Summary. Intrarenal blood flow distribution was evaluated in 60 dogs with radiolabeled microspheres. The range of mean arterial blood pressure ($\overline{BP}$) was 90 to 180 mm Hg, with an average of 137 mm Hg ± 20 (SE). A poor but significant inverse correlation was found between renal blood flow (RBF) per gram kidney weight and the spontaneously occurring mean systemic pressure ($r = -0.24$, $P < 0.001$). Analysis of blood flow rates per gram inner and outer cortex showed substantially lower inner cortical flows in dogs with elevated blood pressure compared to dogs with lower blood pressures; outer cortical flow was essentially equivalent in the 60 animals. The correlation coefficient between inner cortical flow and $\overline{BP}$ was -0.534 ($P < 0.001$). Both inner and outer cortical resistance to flow increased significantly with pressure ($P < 0.001$). Electrolyte excretion rates (Na^+ and K^+) did not vary substantially in this population of dogs. These results demonstrate that spontaneously elevated blood pressure is associated with a specific reduction in inner cortical blood flow.

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