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Intrarenal Hemodynamics in Nonfiltering, Filtering, and Compensated Kidneys[1] (41045)

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Abstract. Renal blood flow and intrarenal blood flow distribution were studied in nine nonfiltering and contralateral compensated kidneys and in seven control filtering kidneys. Unilateral ureteral ligation coupled with a 2-hr renal ischemia 4 days prior to the experiment induced the kidney to be nonfiltering and resulted in a marked decrease in renal blood flow (59.2 ± 35.1 ml/min vs 124.7 ± 12.9 ml/min in control, $P < 0.05$). In contrast, the contralateral kidney demonstrated a compensatory increase in renal blood flow (48%) equal to the reduction in flow to the impaired kidney (52%). Regional blood flows to the four cortical zones were commensurate with the rise in total flow in that they increased markedly in all zones of contralateral kidneys. In nonfiltering kidneys, the decrease in total flow was due to a proportional fall in regional blood flows of zones I, II, and III. Blood flow in zone IV also decreased but not to the extent seen in the other zones. Thus, it may be concluded that the large changes in renal hemodynamics to nonfiltering and compensated kidneys are proportionally distributed throughout the four cortical zones with the exception of an attenuated decrease in blood flow in the innermost zone.

The experimental model of a nonfiltering kidney developed by Blaine *et al.* (1) has been used rather extensively in the past decade in studies of the renin-angiotensin (2–6) and prostaglandin systems (7–9). The rationale is that one is able to study factors that affect renal hormonal systems while eliminating tubular influences that are subsequent to filtration. Although the procedure for rendering the kidney nonfiltering incurs structural as well as functional damage to the organ, the kidney can still change vascular tone in response to various stimuli and continues to secrete renin. Consequently, many studies have utilized the model to investigate mechanisms regulating renin release. It is of interest that several of the experimental manipulations used in those studies frequently cause alterations in regional blood flow (in filtering kidneys), yet there has been no definitive description of intrarenal blood flow distribution in this model. Therefore, the purpose of the present study was to characterize the patterns of intrarenal blood flow distribution in the nonfiltering and contralateral compensated filtering kidneys and compare them with those in normal filtering kidneys.

Methods. Experiments were performed on two groups of dogs of either sex, weighing 11–16 kg. Group 1 contained seven dogs which served as control dogs with normal, filtering kidneys. Group 2 was nine experimental dogs in which one kidney was rendered nonfiltering by the method of Blaine *et al.* (1). Briefly, 4 days prior to the day of the experiment the animals was anesthetized and the left kidney exposed by a retroperitoneal incision using sterile technique. The left ureter was ligated in two places and the renal artery clamped near its origin from the aorta for 2 hr. After this period of ischemia the clamp was removed and the incision sutured. On those occasions where the left kidney presented with a double renal artery, the right kidney was rendered nonfiltering. To assure that the kidneys were indeed nonfiltering, part of the kidney surface was exposed and decapsulated (to visualize tubules) and lissamine green was injected into the renal artery. The failure of the dye to appear in the tubules, after its initial flush in the vascular space, constituted evidence of nonfiltration. On the day of the experiment, the animals were anesthetized with sodium

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pentobarbital (30/mg/kg, iv) and maintained with periodic small doses as needed. The trachea was exposed and cannulated, and each animal was mechanically ventilated with a Harvard respirator. Minute volumes were selected by reference to the normogram of Kleinman and Radford (10). Body temperature was monitored with a rectal temperature probe and maintained at 37° by a circulating water heating pad and a radiant heat lamp when necessary.

Catheters (PE 200) were placed in the femoral artery and vein for measurement of blood pressure (Statham strain gauge, P23Db, Gould Brush recorder 220), blood sampling and to give systemic infusions. A thoracotomy was performed at the left fourth intercostal space, and a catheter (PE 160) was placed in the left atrium for microsphere injection. The dogs were then placed in a metal frame which held them in a position approximating their normal standing posture.

A retroperitoneal flank incision was made to expose the left renal artery for placement of a noncannulating electromagnetic flow probe (Carolina Medical Electronics). The flow probe was calibrated by renal artery cannulation at the end of each experiment.

Intrarenal blood flow distribution was assessed with radioactive microspheres (New England Nuclear), 15.0 ± 1.1 μm in diameter, labeled with γ-emitting nuclides. Four nuclide species, ^{141}Ce, ^{51}Cr, ^{113}Sn, and ^{46}Sc, were randomly used.

Prior to injection, the stock solution of spheres was agitated mechanically and ultrasonicated. Approximately 7×10^5 spheres were withdrawn for the stock solution and suspended in 2 ml of saline warmed to 37°. This sphere solution was then immediately injected into the left atrium and flushed with 10 ml of warmed, heparinized saline. The kidneys were removed at the end of the experiment and the cortex was divided into four equal zones, designated as Zones I–IV, with I being the outermost and IV the innermost cortical zone. The medulla and portions of the cortex in the renal poles, which could not be divided accurately into zones, were treated in the same manner as cortical zones so that total renal blood flow could be evaluated. Tissue samples were weighed and placed at equal heights in 10-cm plastic counting vials. The radioactivity of the samples was measured with a Searle γ-counter and isotope separation as previously described (11).

Blood flow to each zone is expressed in milliliters per minute per gram wet kidney weight. All values are presented as means ± 1 SEM. Analysis of variance was used to test for differences among the three groups. Comparisons between the means were performed with Scheffe t tests.

Results. Renal hemodynamics data for both groups of dogs are presented in Table I. Mean arterial blood pressure was not different between the groups. Renal blood flow was significantly reduced ($P < 0.01$) in the nonfiltering (NF) kidneys and significantly increased ($P < 0.05$) in the contralateral compensated (CC) kidneys compared to control filtering (F) kidneys. The magnitude of the increase in renal blood flow in CC kidneys (48%) matched the decrease in renal blood flow in NF kidneys (52%) such that total flow to both kidneys was not different in control and experimental dogs 250.1 ± 32.2 vs 243.4 ± 20.9 (ml/min), respectively.

A similar pattern is seen with respect to the cortical distribution of renal blood flow (Table I, Fig. 1). The changes in whole kidney blood flow in NF and CC kidneys were distributed throughout the four cortical zones. Blood flow in NF kidneys was markedly lower in cortical zones I, II, and III ($P < 0.01$) compared to controls. The values for absolute blood flow in these zones averaged 44% of control, similar to the decrease in whole kidney blood flow (47%). In zone IV, the same directional change in blood flow (as in other zones) was noted, but the fall was proportionally less (i.e., blood flow was 64% of control). Consequently, the decrease observed was not statistically different from controls. On the other hand, in CC kidneys a significant increase in blood flow was noted in every cortical region ($P < 0.01$). The values for absolute blood flows in these zones were approximately 45% higher than in controls.

TABLE I. RENAL BLOOD FLOWS AND INTRARENAL DISTRIBUTION

	N	MAP (mm Hg)	Absolute renal blood flow		Regional blood flow (ml·min^{-1} g^{-1})			
			ml/min	ml·min^{-1} g^{-1}	I	II	III	IV
			Control					
Group 1								
Filtering (F) kidneys	7	120 ±5	124.7 ±12.9	2.61 ±.29	4.36 ±.50	3.91 ±.47	2.89 ±.46	1.54 ±.34
F vs NF			<0.01	<0.01	<0.01	<0.01	<0.01	NS
			Experimental					
Group 2								
Nonfiltering (NF) kidneys	9	113 ±6	59.2 ±5.1	1.10 ±.13	1.92 ±.35	1.60 ±.30	1.29 ±.14	0.99 ±.21
NF vs CC			<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Contralateral compensated (CC) kidneys	9	113 ±6	184.2 ±21.2	3.92 ±.48	7.17 ±1.03	7.37 ±.97	5.36 ±.62	3.00 ±.31
CC vs F			<0.05	<0.05	<0.05	<0.01	<0.01	<0.01

Note. Values are presented as Means ± SE. N = number of animals. MAP, mean arterial pressure.

Discussion. The present study describes the renal hemodynamic effects of rendering a kidney nonfiltering according to the method of Blaine *et al.* (1). In our experiments, the contralateral kidney remained intact in order to study the compensatory response of this kidney during renal function impairment in the other kidney. We have found, as others have reported (3–6, 9), that the experimental maneuver resulted in a marked fall in renal blood flow to the affected kidney. Interestingly, the decrease in renal blood flow to the nonfiltering kidney was virtually compensated by a striking vasodilation in the contralateral kidney. Both flows were significantly different from renal blood flows in control, filtering kidneys. Furthermore, we have extended our current knowledge by examining the distribution of renal blood flow in the three groups. Regional blood flows were significantly lower in nonfiltering kidneys than in control kidneys in cortical zones I, II, and III. In the innermost zone (IV) blood flow was also decreased though proportionally less than in the outer zones. Whether this reflects some functional preservation remains speculative. In the compensated kidneys, the compensatory vasodilation of whole kidney blood flow was reflected in increases of regional blood flow in every cortical zone.

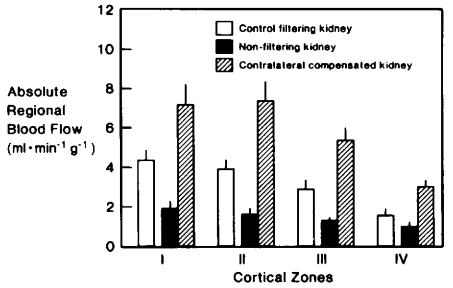

FIG. 1. Comparison of renal cortical blood flow distribution in filtering (n = 7), nonfiltering (n = 9), and contralateral compensated (n = 9) kidneys.

It should be pointed out that, as mentioned earlier, renal and zonal blood flows were calculated per gram wet kidney weight. Since the method for inducing nonfiltration may result in edema formation in the postischemic kidney, the corrected values for renal blood flows may be inappropriately low. In our experiments, however, the increase in weight of the nonfiltering kidney (17%) compared to both control and compensated kidneys, is not enough to account for the 52% decrease in blood flow. Moreover, these changes persisted with

values for total and regional blood flows which were uncorrected for tissue weights.

The assessment of intrarenal blood flow distribution in dog kidneys with the use of 15-μm microspheres has been established by the studies of McNay and Abe (12) and others (13, 14). We have also validated the technique in our laboratory in a previous study (11). Several recent methodological studies have suggested that microspheres are subject to axial streaming and steric hindrance (into afferent arterioles) (15–17) thereby leading to erroneous estimates of blood flow. While acknowledging that the absolute values for cortical blood flow may be subject to a certain degree of uncertainty because of the rheologic properties of the spheres, we are aware of no reported streaming artifact that would substantially alter our findings or compromise our conclusions. Moreover, there are indications that the source of artifact relating to vessel geometry seen in rabbits and rats may not be present in the dog (18, 19). Therefore, it seems reasonable to conclude that the microsphere distributions in the present study are indicative of true changes in blood flow to the various cortical zones and are not merely the result of a streaming artifact.

Intrarenal blood flow distribution in nonfiltering kidneys was previously measured in one study investigating renal prostaglandin production in the dog (8). The intent of the study, however, was to compare the effects of indomethacin, in the presence and absence of arachidonic acid, on fractional zonal blood flow. Consequently, values for absolute regional flow in nonfiltering kidneys and comparisons to normal filtering and contralateral kidneys were not reported. Other studies, although utilizing different models of renal pathophysiologic states, parallel some of the findings in the present study. McNay and Miyazaki (20) observed that the increase in renal blood flow 1 week following unilateral nephrectomy in dogs was proportionally distributed among the four cortical zones, similar to our observation in contralateral, compensated kidneys. Two laboratories investigating chronic unilateral ureteral obstruction in rats (21, 22) reported that blood flow was equally reduced in the outer and inner cortex. In those experiments however, the cortex was divided into only two zones which may have masked a detectable change. Indeed, a study of unilateral ureteral obstruction in dogs (23), wherein the cortex was divided into four zones, found an increase in fractional blood flow in zone IV to the extent seen in the other three zones. Thus, it may be concluded that the large changes in renal hemodynamics to nonfiltering and compensated kidney are proportionally distributed throughout the four cortical zones with the exception of an attenuated decrease in blood flow to the innermost zone.

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