Deep Venous and Lymphatic Vessel Pressures During Renal Autoregulation in the *in situ* Dog Kidney* (33943)

S. GAZITUA,[1] J. B. SCOTT,[2] T. E. EMERSON, JR., AND F. J. HADDY
Department of Physiology, Michigan State University, East Lansing, Michigan 48823

The role of venous resistance in renal autoregulation is a controversial subject. From measurements of deep venous pressure, some investigators concluded that the changes in total renal vascular resistance result predominantly from alterations in venous resistance (1–3), the latter being mediated through changes in tissue pressure. In contrast, other investigators, using similar techniques for measuring deep venous pressure, concluded that the role of venous resistance is minimal in the autoregulatory response (4, 5). Also, it has been reported that neither proximal tubular pressure nor peritubular capillary pressure change appreciably when arterial blood pressure is elevated over the range 90–200 mm Hg (6). In none of the studies, however, was autoregulation elicited by locally altering renal perfusion pressure with the kidney *in situ*. Perhaps relevant is the observation that the pressure in a renal hilar lymphatic vessel, possibly a better index of tissue pressure than deep venous pressure, is little influenced by arterial pressure during *in situ* perfusion (7, 8).

The purpose of the present study was to measure deep venous pressure and hilar lymphatic vessel pressure simultaneously in the *in situ* kidney during autoregulation elicited by either a local change in renal artery pressure or renal blood flow.

Methods. The studies were performed in anesthetized (sodium pentobarbital, 33 mg/kg) dogs whose blood was rendered incoagulable with heparin sodium. In experiments in which renal perfusion pressure was the controlled variable, a precalibrated blood pump was interposed between the left renal and right femoral arteries. The outflow side of the pump circuit consisted of two branches; one branch fed the renal artery; the second branch, which contained a Starling resistor, was connected to a femoral vein. Hence, renal perfusion pressure could be manipulated by altering the resistance of the second branch. The renal vein was cannulated and its outflow was diverted into a reservoir from which it was returned to the animal via a second pump. Renal blood flow was determined by collecting timed volumes from the renal vein. In the experiments in which renal blood flow was the controlled variable, the Starling resistor branch of the pump outflow system and the venous reservoir were deleted. The renal perfusion pump was precalibrated and renal venous outflow was diverted directly into the jugular vein. In all the experiments, deep renal venous pressure was measured through a polyethylene catheter (o.d. 0.9 mm) which was advanced retrogradely up the renal vein until the tip lay in the cortex (the exact position of the catheter tip was determined at autopsy). A polyethylene catheter (o.d 0.6 mm) was inserted into a hilar lymphatic vessel (7, 8). Collateral blood and lymphatic vessels remained intact. Pressures in the renal artery, lymphatic vessel, large and small vein were monitored via Statham transducers. Total renal vascular resistance (R_T) was divided into series resistances (R_I and R_{II}) as follows:

$$R_T = \frac{\text{renal artery pressure} - \text{large vein pressure}}{\text{total renal blood flow}},$$

$$R_I = \frac{\text{renal artery pressure} - \text{small vein pressure}}{\text{total renal blood flow}},$$

$$R_{II} = \frac{\text{small vein pressure} - \text{large vein pressure}}{\text{total renal blood flow}}.$$

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[1] International Postdoctoral Research Fellow TW1182 from the National Institutes of Health, U. S. Public Health Service.

[2] Established Investigator of the American Heart Association.

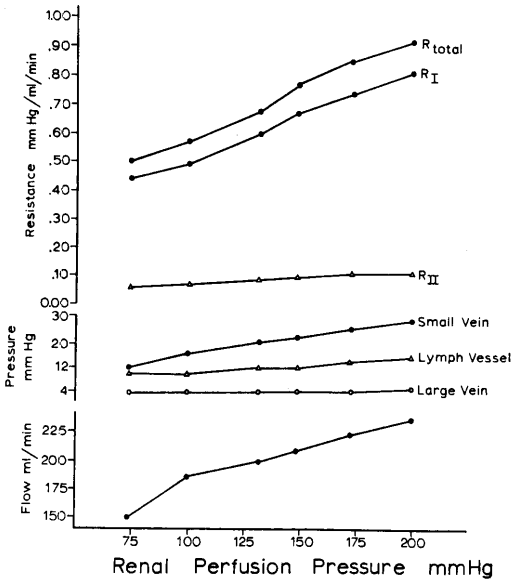

FIG. 1. Effect of local stepwise increases in renal perfusion pressure on renal resistances, blood flow, and small vein and lymphatic vessel pressures ($N = 8$).

It is apparent that the validity of resistances I and II rest on the assumption that the small vein pressure used accurately reflects the pressure in all renal veins of a similar size. This would be the case if (i) changes in total renal blood flow are equally distributed throughout the renal substance, and (ii) there are sufficient functional vein to vein anastomoses upstream to the small vein catheter tip to insure measurement of a true lateral pressure. The rationale for using lymphatic vessel pressure as an index of renal tissue pressure was presented in a previous communication (7). Statistical analysis of the data was by the Student's t test modified for paired replicates.

Results. Data presented are from experiments in which the tip of the small vein catheter was shown at autopsy to be in the renal cortex and in which total vascular resistance rose as a function of renal perfusion pressure or renal blood flow. Figure 1 presents the average effects of stepwise increases in renal perfusion pressure on renal resistances, pressures, and blood flow. It is apparent that changes in renal perfusion pressure over the range 70–200 mm Hg produced only small changes in renal venous and lymphatic vessel pressures. Renal blood flow rose proportionately less than perfusion pressure; hence total renal resistance progressively increased. The rise in total resistance resulted from a rise in both resistances I and II. However, 88% of the increase in total resistance was due to a rise in resistance I.

In some of these experiments perfusion pressure was suddenly elevated from a low (>100 mm Hg) to a high (<175 mm Hg) level and held constant at the high level for several minutes. Serial venous outflow measurements were begun immediately after reaching the high pressure. In 2 of 7 experiments, a gradual decline in flow occurred during the period of constant high pressure. In these experiments, the fall in flow was associated with simultaneous falls in small vein and lymphatic vessel pressures. Thus, in these experiments, venous and lymphatic vessel pressures fell at the same time total renal resistance rose. During this period the rise in total resistance was due in its entirety to a rise in resistance I; resistance II did not change.

The effects of acute stepwise elevations in renal blood flow on renal pressures are shown in Fig. 2. It is apparent that in each experiment all pressures increased as a function of the blood flow. Over the flow ranges studied, average rises in perfusion, small vein and lymphatic vessel pressures were 196, 26, and 16 mm Hg, respectively. An intra-individual comparison failed to show any difference between the increase in small vein pressure and the increase in lymphatic vessel pressure. In every experiment total resistance to flow was greater at the final flow than at the initial flow indicating renal autoregulation (Table I). As in the previous series of experiments, the rise in total resistance was entirely or largely due to a rise in resistance I. Resistance II was affected irregularly, rising in 3 experiments, falling in 3 and not changing in 1. On the average, resistance I increased 180% while resistance II was not affected.

The effect of acetylcholine on renal perfusion, small vein and lymphatic vessel pressures during autoregulation was studied in

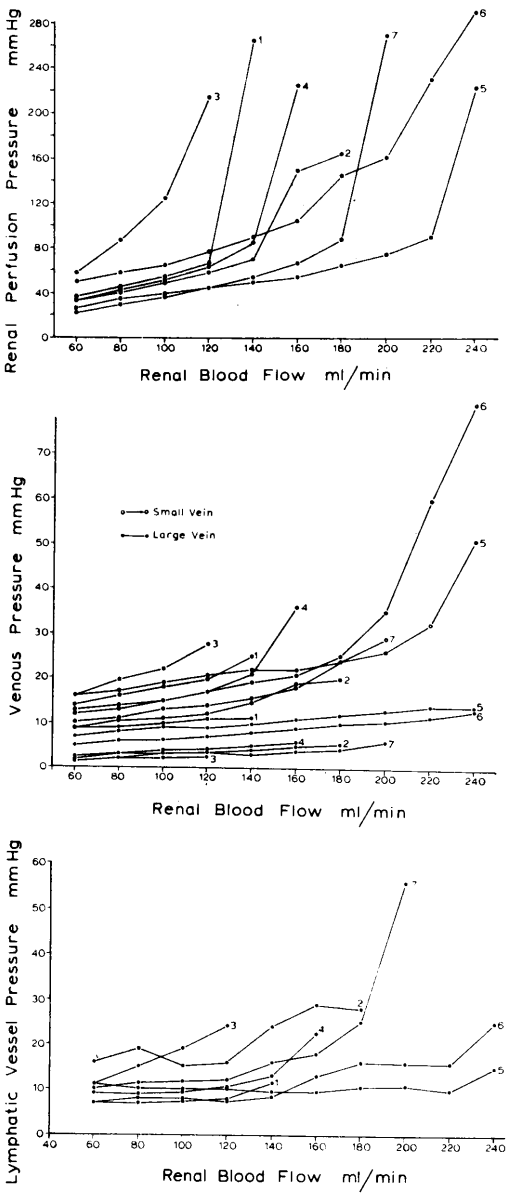

FIG. 2. Effect of local stepwise increases in renal blood flow on renal perfusion, small and large vein and lymphatic vessel pressures; no. correspond to different experiments ($N = 7$).

the constant flow perfusion experiments. In 5 experiments, 0.5 ml of an isotonic solution of acetylcholine chloride (40 μg/ml) was injected into the renal artery at the height of the autoregulatory response. On the average the injection was associated with reductions in mean perfusion, small vein and lymphatic vessel pressures of 51, 8 and 7%, respectively. While lymphatic vessel pressure fell in all the experiments, small vein pressure decreased in 3, did not change in 1, and increased in 1.

Discussion. The results of the present study do not support the concept that changes in venous resistance, brought about by alterations in intrarenal pressure, play a major role in renal autoregulation. Resistance changes, in the *in situ* kidney, elicited either by a local alteration in blood flow or perfusion pressure were located primarily in the vascular segment upstream to the site of the small vein catheter. Furthermore, the failure of either deep venous pressure or hilar lymphatic vessel pressure to change markedly in the face of large changes in renal perfusion pressure or blood flow suggests that neither maneuver greatly affects intrarenal pressure. Thus, though the studies shed no light on the ultimate mechanism responsible for renal autoregulation they do indicate that the site of the response is proximal to the large intrarenal veins and that it probably involves an active rather than a passive mechanism. The latter is supported by the effects of acetylcholine on renal perfusion, small vein and lymphatic vessel pressures. Acetylcholine markedly reduced perfusion pressure but it only slightly decreased small vein and lymphatic vessel pressures.

While the failure of deep venous pressure to change greatly during renal autoregulation is consistent with some earlier studies (4–6), it is inconsistent with others (1–3). In the latter studies, emphasis was placed on proper positioning of the deep venous catheter. It was pointed out that unless the tip of the catheter was advanced into an arcuate or interlobular vein the rise in venous resistance would be missed (2). Indeed the criticism of improper catheter placement has been leveled by Hinshaw (2) at one investigator who failed to record large changes in small vein pressure during renal autoregulation. For this reason, care was taken in the present studies to avoid this criticism (see "Methods"). It should be emphasized, however, that technical differences do exist between the present and previous investigations

TABLE I. Effect of Increasing Renal Blood Flow (RBF) on Total Vascular Resistance (RT), Resistance I and Resistance II (mm Hg/ml/min).

	R_T		R_I		R_{II}		RBF	
Expt.	Initial	Final	Initial	Final	Initial	Final	Initial	Final
1	0.49	1.80	0.40	1.71	0.09	0.10	60	140
2	0.56	0.88	0.43	0.81	0.13	0.08	60	180
3	0.93	1.77	0.68	1.56	0.24	0.21	60	120
4	0.51	1.32	0.33	1.13	0.18	0.19	60	160
5	0.33	0.87	0.18	0.72	0.15	0.15	60	240
6	0.75	1.13	0.63	0.85	0.12	0.29	60	240
7	0.35	1.32	0.22	1.21	0.13	0.12	60	200
Mean	0.56	1.30[a]	0.41	1.14[a]	0.15	0.16	60	183

[a] $p < 0.01$ when compared to initial value.

dealing with autoregulation in the *in situ* kidney. First, the changes in renal perfusion pressure reported here were accomplished without effects on the animal's systemic blood pressure. This is in contrast to earlier investigations where alterations in renal perfusion pressure were produced by manipulation of aortic pressure (1–3, 5, 6). Under the latter condition it is possible that both local and remote circulatory controlling systems are involved in the autoregulatory response. Second, in the present studies, all renal collateral vessels (arteries, veins, and lymphatics) were left intact; this was not the case in previous investigations (1, 2). Interference with normal lymphatic and venous drainage from the kidney might be conducive to the production of abnormal renal pressures or blood flow.

Summary. Autoregulation evoked by alterations in renal blood flow or renal arterial pressure to the *in situ* collateralized kidney was associated with only small changes in deep renal venous pressure and renal hilar lymphatic vessel pressure. Resistance calculations suggest that the change in resistance during renal autoregulation occurs predominantly in vessels upstream to the arcuate or intralobular veins. Thus, the present study fails to provide support for the "tissue pressure" hypothesis of renal autoregulation in the intact collateralized kidney.

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