Constriction of the Renal Vein—A New Concept in Renal Hypertension *

JOHN R. DERRICK, M.D., VAN REA, M.D., TRUMAN G. BLOCKER, M.D.

From the Department of Surgery, The University of Texas Medical Branch, Galveston, Texas

ACCORDING to current concepts systemic hypertension often occurs as a result of renal ischemia.[5-7] Previous investigators have found a high incidence of systemic hypertension and renal ischemia secondary to decreased blood flow to the kidney.[4] This study was conducted to determine whether the same phenomenon occurs with a decrease in blood flow from the kidney, that is, with increased renal venous pressure.

Material and Methods

Ten mongrel dogs were used in the study. Unilateral nephrectomies were performed through a flank incision made on the left side in each animal. After recovery, which averaged about two weeks, a midline incision was made and the right renal vein and its collaterals were completely exposed. The renal vein was constricted with 3–0 silk suture to reduce its size approximately 60 to 80 per cent. It was then necessary to ligate all collaterals. Special care was taken to locate the capsular collaterals. In eight of ten dogs, only gonadal and capsular venous collaterals were found. In the other two dogs, both females, ovarian, suprarenal, and capsular collaterals were found.

In each dog, flow studies were made before and after constriction; oxygen tension measurements were recorded in the kidney parenchyma before and after constriction, and also at termination of the experiment; venous pressures were determined before and after constriction; arterial pressures were taken throughout the duration of the experiment; and venograms were made just before termination of the study to observe the constriction.

Blood Flow Measurements

Blood flow was measured with a square-wave electromagnetic flow meter. Very accurate recordings of both pulsatile and mean flow can be obtained by using an instrument of this type.[2, 3, 8] The electromagnetic flow meter is based on the magnetic induction principle which states that if a conductor passes through a magnetic field in such a direction as to cut the lines of magnetic force there will be a voltage generated in the conductor at right angles to the direction of motion and the magnetic field. The magnitude of this voltage depends on the velocity of the conductor, the dimensions of the conductor, and the strength of the magnetic field. These variables directly affect the number of magnetic lines of force that are cut per unit time.

The problems in design of the electromagnetic flow meter for use on unopened blood vessels are related to the small voltage generated in the conductor and the electrical interference caused by such factors as cardiac potentials, electrode polarization voltages, and static voltages generated by rubbing metal surfaces. These

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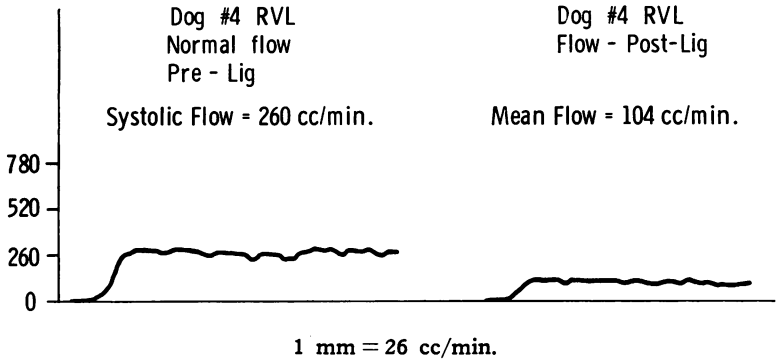

FIG. 1. Flow recorded by use of electromagnetic flow meter. This is an illustration of a typical reduction of preconstriction to postconstriction flows.

problems of interference have been minimized by the development and advancement of the square wave electromagnetic flow meter.

The voltage generated in the conductor is picked up by a magnetic probe, which is, essentially, an electromagnet. The vessel is grasped between the poles and held in contact with a pair of electrodes which pick up the signal from the conductor. This signal is amplified and distinguished from the interferences mentioned and then recorded on any standard recorder.

Flow in the renal vein was measured before and after constriction. Before constriction the collaterals to the renal vein were tied and the probe placed around the vessel approximately 2 cm. from the junction with the vena cava and the flow recorded. The vessel was then constricted approximately 2 cm. from the kidney and flow was again recorded from the same position.

Venous Pressure Recordings

Pressures were recorded in the renal vein both before and after constriction. A 20-gauge needle was inserted into the vein and the pressure was determined using a low-pressure transducer. The increased venous pressure at times made it difficult to stop the bleeding from the needle puncture.

Arterial Pressure Determinations

For recording of arterial pressure, a pediatric blood pressure cuff attached to a mercury manometer was used. The cuff was applied to the proximal portion of the dog's tail. Pressures were taken after applying pressure until a pulse was no longer felt in the caudal artery and then allowing the pressure to decrease until the pulse could be felt again.

An average of three pressure recordings was taken as the arterial or caudal pressure. To validate the results, pressures were compared with an original arterial pressure and one taken on a strain gauge manometer. The pressures taken in the aorta agreed closely with the caudal pressures.

Oxygen Tension Measurements

The oxygen tension was measured by a polarograph with a Beckman Oxygen

TABLE 1. *Mean Flow Through Renal Vein* (cc./min.)*

Dog	1	2	3	4	5	6	7	8	9	10
Normal	147	279	186	260	250	180	167	204	148	241
Postconstriction	84	93	50	93	90	55	54	37	30	93

* Flow (both normal and post constriction), was recorded in each of ten dogs after performing a nephrectomy of the left kidney and later constricting the contralateral renal vein. These dogs were followed for a period of 86 days.

TABLE 2. *Renal Venous Pressure* (mm. of Hg)*

Dog	1	2	3	4	5	6	7	8	9	10
Normal	20	18	18	24	19	33	21	20	21	21
Postconstriction	27	28	24	34	28	37	26	30	22	36

* Renal venous pressure (normal and post constriction) was recorded in each of ten dogs after performing a nephrectomy of the left kidney and later constricting the contralateral renal vein. These dogs were followed for a period of 86 days.

Micro-electrode.[1] This micro-electrode is made of a 0.005-inch platinum wire cathode sealed in glass so that only the tip is exposed and which is cemented within a silver tube, which acts as the anode. A thin polyethylene membrane, permeable to gases, covers the tip of the anode and traps between it and the cathode an electrolyte solution. This electrode fits into a Riley arterial needle to allow measurements of oxygen tension to be made *in vivo*.

The current generated by the electrode is directly proportional to the rate of reduction of oxygen at the cathode. This current is amplified and recorded and provides continuous measurements of oxygen tension. Oxygen tensions were taken in the kidney tissue in the medullary region near the hilus on the ventral side by placement of the Riley needle and electrode. Oxygen tensions were taken before and after constriction in generally the same area.

Other Studies

At termination of the project, the dogs were sacrificed and the kidneys examined histologically.

In a subsequent study, another group of five dogs were studied under the same conditions as the first group but with an additional study of blood and urine chemistry.

Results

The typical flow pattern both before and after constriction is shown in Figure 1. For this animal, Dog 4, the damping of the systolic and diastolic pressure peaks into a mean flow after constriction, as would be expected. There is, of course, an overall decrease in the mean flow. Pre-ligation flow in all the animals averaged 205 cc./min. After constriction, the flow was reduced to an average of 33 per cent of the preconstriction readings. Flow changes for the ten dogs are shown in Table 1.

TABLE 3. *Blood Pressure of Renal Vein Constriction Series* (mm. of Hg)*

Dog	1	2	3	4	5	6	7	8	9	10
Date										
Aug. 7, 1962	140	138	148	128	130	145	152	140	135	138
13, 1962	135	135	Died	140	Died	145	144	Died	Died	154
14, 1962	138	146	2 days	132	2 days	138	154	3 days	6 days	134
22, 1962	148	156	postop	158	postop	168	154	postop	postop	138
29, 1962	150	135		165		158	144			150
Sept. 12, 1962	150	160		170		160	158			151
16, 1962	143	168		163		163	163			148
Oct. 2, 1962	183	180		185		170	155			163
7, 1962	191	178		189		185	172			171
12, 1962	190	183		200		187				
19, 1962	188	185		193			189			192
Nov. 1, 1962	185	190		190		180	190			190

* Follow-up arterial blood pressure was recorded in each of ten dogs after performing a nephrectomy of the left kidney and later constricting the contralateral renal vein. These dogs were followed for a period of 86 days.

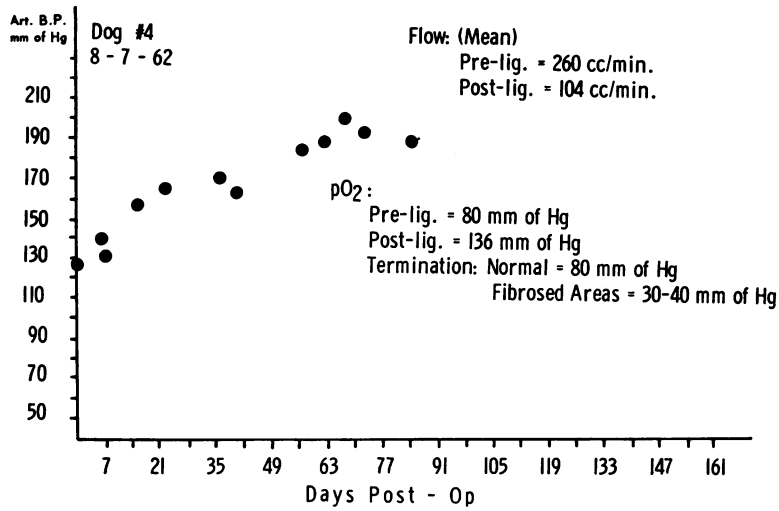

FIG. 2. Arterial B.P. was followed in each dog for 86 days. This is an example of a typical dog showing a gradual increase in blood pressure. Flows and O_2 tension on this dog are also given.

The venous pressure recordings are shown in Table 2. The venous pressures increased from an average of 21.5 mm. Hg to 29.2, an average increase of 36 per cent.

After venous constriction, a total of 11 arterial pressure readings were made during a period of approximately 90 days (Table 3). An average blood pressure rise of 49.2 mm. Hg was observed. Figure 2 shows results in a typical example (Dog No. 4). This animal had an original pressure of 128 mm. Hg, and 86 days after constriction, the pressure was 190 mm. Hg. In this particular instance, the blood flow had been reduced from 260 cc./min. before constriction to 93 cc./min. after constriction, with an increase in renal venous pressure from 24 to 34 mm. Hg on the lateral side of the constriction.

Oxygen tension changes are given in Table 4. Before constriction oxygen tension in the apparently normal kidney parenchyma varied from 40 to 144 mm. Hg. In measurements made after constriction, greater variations in results were found. In some animals, the original value became doubled, in some, the readings stayed the same, and in others, the oxygen tensions were lowered. When the oxygen tensions were recorded at termination of the project, the readings ranged from 40 to 84 mm. Hg in some areas, but in others were decreased to 16 to 38 mm. Hg range, and this was assumed to denote nonviable tissue. This assumption was verified by histologic study. Histologic examination of the kidney tissue showed evidence of chronic hypertension with thickened walls of the arterioles and

TABLE 4. *Average Oxygen Tension Recorded in Renal Parenchymal Tissue of Unilaterally Nephrectomized Dogs* (mm. of Hg)*

Dog	1	2	3	4	5	6	7	8	9	10
Normal (pre-const.)	75	60	65	80	70	40	70	66	74	144
Immediate (post-const.)	90	60	70	136	75	24	100	80	90	80
Termination (viable)	60	66		80		40	84			60
Termination (non viable)	38	16		35		18	30			30

* Oxygen tensions of the renal parenchyma (normal, termination showing viable and nonviable) was recorded in each of ten dogs after performing a nephrectomy of the left kidney and later constricting the contralateral renal vein. These dogs were followed for a period of 86 days.

TABLE 5.

Serum Level	Norm	5-2-63	5-6-63	5-9-63	5-12-63	5-16-23	5-20-63	5-23-63
K_1*	4.7	5.3			Died 8 days postop			
K_2	4.3	4.9	5.6	5.3	5.0	4.8	5.2	5.6
K_3	5.5		4.4	3.4	5.0	5.1	5.3	4.7
K_4	5.2	5.4	5.1	6.2	5.6	5.6	5.3	4.7
K_5	4.8	6.5			Died 6 days postop			
Na_1	149	147			Died 8 days postop			
Na_2	145	153	146	150	150	144	150	153
Na_3	145		143	158	159	147	150	154
Na_4	151	152	147	160	163	153	150	154
Na_5	149	146			Died 6 days postop			
CO_{21}	26	20			Died 8 days postop			
CO_{22}	24.5	22.5	22.7	24	25.3	21.8	24.7	24.7
CO_{23}	24		18.7	22	22.8	21.8	26.0	24
CO_{24}	25	21.5	21	25.5	22.8	22.2	26.0	29
CO_{25}	23	20.5			Died 6 days postop			
Cl_1	112	110			Died 8 days postop			
Cl_2	111	116	110	110	117	110	110	107
Cl_3	110		114	117	120	111	111	109
Cl_4	110	111	108	123	114	114	112	109
Cl_5	114	92			Died 6 days postop			
A/G_1	2.9/2.3	3.1/2.5			Died 8 days postop			
A/G_2	2.5/3.1	2.8/3.2	2.3/3.3	2.2/3.2	3.2/3.5	2.3/2.9	2.5/3.3	2.1/3.0
A/G_3	2.8/2.5		2.0/3.2	2.1/4.1	2.6/3.2	2.3/3.3	2.5/3.2	1.6/3.2
A/G_4	3.6/3.0	3.5/3.2	2.8/3.0	3.1/3.1	3.6/3.5	3.3/2.5	3.1/2.8	2.0/3.2
A/G_5	2.1/4.8	2.4/4.0			Died 6 days postop			
BUN_1	14	75			Died 8 days postop			
BUN_2	28	60	55	42	68	50	53	52
BUN_3	19		95	62	48	35	34	30
BUN_4	18	13	22	24	18	20	20	17
BUN_5	30	190			Died 6 days postop			
Urine								
$Protein_1$	++	+++			Died 8 days postop			
$Protein_2$	0	++	+	+	Trace	+	++	+
$Protein_3$	0	++	++	+++	− − −	++	++	+
$Protein_4$	+	+	+	++	++	+++	++	+
$Protein_5$	+	+++			Died 6 days postop			

* Subscript implies the dog number.

Blood and urine studies were run on each of 5 dogs with nephrectomies and constriction of the contralateral renal vein. The above shows the results of such studies compiled after a one month period.

some ischemic glomeruli, tubular degeneration, and areas of extensive fibrosis.

The results of serum and urine studies are shown in Table 5. Considerable loss of protein in the urine occurred after constriction of the vein, and albumin-globulin (AG) ratios showed a tendency toward reversal. It is interesting that these same urine findings are often seen in nephrosis.

Discussion

Findings from these studies suggest that outflow obstruction may in some instances be a cause of reduced blood flow to the kidney. An additional factor which could contribute to ischemia is the increased tissue pressure which results from venous occlusion. The counterpart of this, in a more common clinical area, is the ischemic ulcers observed in patients with chronic stasis edema of the lower extremity, for these ulcers are thought to be caused by ischemia.

There are numerous conditions which may result in transient or permanent secondary increased renal vein pressure on the basis of increased intraperitoneal pressure, for example, ascites, rapid gain in weight,

pregnancy, abdominal binders, etc. Elevated venous pressure after heart failure seems, in most instances, to cause back pressure in the renal vein. A great deal of clinical study will be required, however, to define the effects of increased renal vein pressure as a potential cause of hypertension and to explain the adverse effects on renal function that may be secondary to increased renal pressure.

Summary

Animal experiments were designed to determine whether systemic hypertension and renal ischemia, known to develop secondary to decreased blood flow to the kidney, would result from increased renal venous pressure or decreased flow from the kidney. The experiments in which blood flow was artificially decreased have been described and the results given.

The effects of venous constriction were observed and the animals destroyed so that histologic examination of renal tissue could be made. Fibrotic development, tubular degeneration, ischemic glomeruli, and thickening of the walls of the arterioles attested to the development of chronic hypertension.

Acknowledgment

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Discussion

Dr. Francis D. Moore (Boston): When I saw this paper on the program I did not know just what shape it was going to take! I think it raises two extremely interesting points.

First, as pointed out in the studies of Ganong and others, the hypertension associated with renal arterial stenosis appears to be due to hypotension in the proximal arteriole of the glomerulus, permitting it to collapse down and literally squeeze out the renin from the juxtaglomerular cells. Therefore this work is a very interesting and conflicting experiment; hypertension has resulted from a situation in which intravascular pressure in the kidney is *increased* rather than decreased.

Secondly, it has been shown by many people, particularly by Dr. Harrison, and Dr. Crocker of our service, that in renal artery stenosis there is hypertrophy of the juxtaglomerular cells. Angiotensin not only affects blood pressure but also produces an immediate response in the adrenal cortex with an outpouring of aldosterone, affecting the excretion of sodium, and therefore the ECF volume.

Therefore, I would like to ask if venous occlusion also produces hypertrophy of the juxtaglomerular cells, since, if it does, we have to make a new theory!

Dr. Florindo A. Simeone (Cleveland): I want to comment on three observations which