Measurement of Renin in Both Renal Veins

Its Use in Diagnosis of Renovascular Hypertension

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THE RECENT development of a simple reliable method for measuring plasma renin activity, together with the availability of a safe procedure for obtaining samples of blood from both renal veins, has prompted us to assess the utility of such measurements in the diagnosis of surgically correctable renovascular hypertension. Previous studies of this type have been reported by McPhaul,[1] Fitz,[2] Kirkendall,[3] and Ueda,[4] and their associates.

A series of 22 patients, diagnosed by conventional measures as having renovascular hypertension, were subjected to operative treatment. Proof of the diagnosis was considered to be established if there was unquestionable improvement in blood pressure after corrective surgery. This is a report of the measurements of renin activity in blood plasma specimens obtained from both renal veins preoperatively and, whenever possible, postoperatively. In addition, plasma renin activity in effluent blood from both kidneys was measured in 13 patients with "essential" hypertension, who were not subjected to operation.

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Patients

Hypertensive patients, ranging in age from 4 months to 66 years were referred to the staff of Vanderbilt University Hospital for consideration of possible renovascular disease. Antihypertensive therapy had been withdrawn at least ten days prior to the study. Screening tests were performed to exclude patients with pheochromocytoma, Cushing's syndrome, or coarctation of the aorta. The preoperative diagnosis of renovascular hypertension was established[5] on the basis of excretory urograms, radiocative iodine (^{131}I) renograms, split renal function studies, abdominal aortograms, and selective renal arteriograms. The diagnosis of "essential hypertension" was based on the same diagnostic studies and the absence of evidence of renal artery stenosis or unilateral renal parenchymal disease.

Laboratory Procedures

Preoperative blood samples were obtained via a catheter placed in the renal veins and inferior vena cava by the Seldinger technique.[6] The position of the catheter was confirmed by injecting a small amount of contrast medium. At operation blood samples were collected by direct venipuncture. Samples of 15 to 20 ml each were drawn from the right and left renal veins and inferior vena cava at the point of its bifurcation. The samples were collected in tubes containing 0.3 ml of 9% ammonium edetate (EDTA) as anticoagulant, placed in ice, and centrifuged in the cold; the plasma was separated and stored at —20 C until extraction. Plasma renin activity was extracted and

Table 1.—Data on Patients with "Essential Hypertension"

Patient No.	Age/Race/Sex	Sodium Diet	Plasma Renin Activity *				Blood Pressure, mm Hg
			RRV	LRV	IVC	Ratio	
1	44/N/M	Low	265	260	231	1	150/100
2	23/W/F	High	314	459	297	1.4	170/115
3	35/W/F	High	530	428	391	1.2	170/100
4	66/N/M	High	368	372	305	1	150/90
5	38/W/F	High	427	429		1	160/120
6	43/W/F	Low	603	641	660	1.1	190/110
7	28/W/M	High	474	380	502	1.2	170/110
8	13/W/F	Low	516	614	740	1.2	160/110
9	45/W/M	High	215	315		1.4	160/100
10	38/N/M	Low	212	227	245	1.1	160/110
11	49/N/M	High	645	694	530	1.1	140/95
12	51/N/M	High	284	316	210	1.1	180/100
13	39/W/M	Low	398	665	329	1.7	145/90

* RRV, right renal vein; LRV, left renal vein; IVC, inferior vena cava.

measured by the method of Boucher and associates[7] as modified by Gordon and coworkers[8] and is reported in nanograms (ng) of angiotensin per 100 ml plasma, generated during a three-hour incubation period. The term "plasma renin activity" (PRA) instead of "renin" has been used since the question of possible accelerators or inhibitors of renin activity was not investigated.

Results

Renal Venous Plasma Renin Activity in Patients With Essential Hypertension.—Thirteen hypertensive patients without roentgenographic evidence of renal artery stenosis were studied as shown in Table 1. Five were on low sodium diet and the rest were on liberal sodium diet during the study. The plasma renin activity in renal venous blood ranged from 212 to 694 ng/100 ml. The ratio of plasma renin activity between the right and the left renal vein (or vice versa) ranged from 1 to 1.4 with one exception, patient 13, in whom the ratio was 1.7.

Renal Venous Plasma Renin Activity in Patients With Unilateral Renal Artery Stenosis (Table 2).—Since the object of the present study was to assess the validity of the individual renal vein plasma renin activity determinations in the diagnosis of renovascular hypertension, these determinations were not correlated with the remainder of the data except in retrospect. A tentative diagnosis of renovascular hypertension was made in 22 cases (14 to 35 in Table 2) when the preoperative studies were indicative of a functionally significant renal artery stenosis. The diagnosis required roentgenographic demonstration of the stenosis and evidence of functional significance on split renal function study. The diagnosis was confirmed in cases 14 to 26 by cure of the hypertension and in cases 27 to 31 by distinct improvement of the hypertension following nephrectomy or unilateral renal artery reconstruction. In three cases (32 to 34) the preoperative diagnosis was not confirmed since the hypertension was unchanged postoperatively. In case 35 there was bilateral renal artery stenosis; unilateral corrective surgery did not effect a cure, but bilateral surgery did effect a cure of the hypertension.

Retrospectively, an attempt was made to correlate the plasma renin activity values with the final diagnoses (Table 2). In 17 of the 18 cases of proven unilateral renovascular hypertension, the preoperative determinations of plasma renin activity had shown a distinct disparity between the right and the left renal vein values. The ratios in various patients ranged from 1.5 to 10; in all 17 cases the higher value was found in the effluent blood from the affected kidney. In two of the three cases in which the

Table 2.—Data on Patients With Preoperative Diagnosis

Patient No.	Age/Race/Sex yr	Sodium Diet	Plasma Renin Activity * Preoperative RRV	LRV	IVC	Ratio	Postoperative RRV	LRV	IVC	Ratio
14	0.4/W/M	Low	7,192	10,867	4,459	1.5				
15	16/W/F	High	133	263	143	1.9				
16	45/W/M	High	145	320	462	2.2				
17 †	61/W/M	High	384	675	376	1.8				
18	51/W/M	High	2,830	9,710	2,945	3.5				
19	29/N/F	High	302	146	205	2.1				
20	31/W/F	High	349	870	376	2.5				
21 †	43/W/F	High	23,700	5,500	7,825	4.3				
22 †	63/W/F	High	588	1,355		2.3				
23	27/W/F	High	1,850	1,790	1,860	1				
24 †	42/W/M	High	1,035	2,187	757	2.2	165	135	160	0.8
25 †	49/W/M	High	1,215	2,290	1,750	1.9	133	142	125	1.1
26	51/W/M	High	1,120	545	560	2.1	232	242	88	1
27 †	4/W/M	High	64,684	25,622	40,119	2.5				
28 †	56/W/M	High	3,898	38,250	1,645	10				
29	56/W/M	High	1,828	2,760	1,735	1.5				
30	59/W/F	High	2,700	5,125	2,775	1.9				
31 †	51/W/F	High	2,400	709	195	3.4				
32	41/W/F	Low	420	919	398	2.2				
33	51/W/F	High	112	158	122	1.4				
34	57/W/F	High	94	109		1.2				
35	43/W/M	High	800	814	470	1	490	149	176	3.3
							260	235	210	1.1

* RRV, right renal vein; LRV, left renal vein; IVC, inferior vena cava; RRA, right renal artery; LRA, left renal artery.
† Preoperative samples obtained at surgery.

postoperative course failed to confirm the preoperative diagnosis of hypertension due to unilateral renovascular disease, the plasma renin activity values had been approximately equal on the two sides prior to operation.

Determinations of plasma renin activity in effluent blood from both kidneys were done several weeks after operation in three patients (24 to 26) with unilateral renal artery stenosis. Prior to operation each patient had shown a distinct disparity between the left and the right renal vein values. After surgical correction of renal artery stenosis, the disparities disappeared, and the patients were completely relieved of their hypertension.

One patient (35) had bilateral renal artery stenosis. Preoperatively, his renal effluent plasma renin activity values were elevated to the same degree on both sides. He underwent a two-stage surgical correction of his renal artery stenosis. Correction of the renal artery stenosis on the left side resulted in a decrease in plasma renin activity in the renal effluent of that side, resulting in a disparity between the two sides. The patient's hypertension persisted. Finally, after correction of the stenosis of the right renal artery, the disparity between the two renal effluent plasma renin activity values disappeared, and the patient became normotensive.

Comment

The concept that the determination of plasma renin activity in the two renal veins might be of diagnostic value in renovascular hypertension is not new.[2-4]

of Renovascular Hypertension

Operation	Blood Pressure, mm Hg		Follow-Up Period in Months
	Preop	Postop	
Left nephrectomy	180/100	100/60	24
Left nephrectomy	140/100	115/75	18
Left nephrectomy	180/120	140/85	4
LRA graft	180/110	130/70	13
Left nephrectomy	200/120	140/85	11
RRA graft	210/130	120/75	10
LRA graft	180/120	125/75	10
RRA graft	170/110	130/75	8
LRA graft	180/120	120/80	8
Right nephrectomy	200/140	120/80	4
LRA repair	160/115	120/80	20
LRA graft	200/120	135/80	6
RRA graft	180/110	135/85	4
Right nephrectomy	170/140	110/80	6
Left nephrectomy	220/120	150/95	2
Left nephrectomy	245/130	180/100	13
Left nephrectomy	200/120	150/90	4
Right nephrectomy	180/100	150/95	16
Left nephrectomy	210/130	200/120	19
RRA graft	190/110	190/110	9
RRA graft	175/100	180/100	4
LRA graft	200/120	170/105	2
RRA graft	170/105	135/85	6

However, the various series of cases published previously have been much smaller than the present one, so that one could not draw a general inference with great confidence. The almost perfect correlation between the clinical and laboratory findings in the present series of cases suggests that this diagnostic procedure can be very helpful in the evaluation of the hypertensive patient. In the present series of 35 cases, anomolous results were observed in only two. Of the 22 patients who underwent renal surgery for supposed renovascular hypertension, the therapeutic efficacy of the operation could have been predicted on the basis of the renal effluent plasma renin activity determination in all but two cases. In one of these (23), the plasma renin activity was elevated on both sides preoperatively, but the patient became normotensive after unilateral nephrectomy. In the other (32), the plasma renin activity was distinctly higher in the left renal effluent than in the right, but the patient remained hypertensive after the removal of the left kidney. Unfortunately, further study of these two cases was precluded by the nature of the surgical procedure.

If, in a case of hypertension, plasma renin activity values on the two sides show a marked disparity (a ratio greater than 1.5), one may suspect that the hypertension is a consequence of an abnormality of the kidney on the side showing the higher value. Removal of the kidney or correction of stenosis of the renal artery on that side can be expected to have a beneficial effect on the blood pressure.

If, in a case of renal artery stenosis (proved by arteriography), there is no disparity in the plasma renin activity values in the two renal veins, one may suspect that the hypertension is not due to unilateral renal disease. Either the hypertension might be due to extrarenal disease, in which case correction of the renal artery stenosis will be of no help, or the hypertension might be due to bilateral renal disease, in which case unilateral correction of renal artery stenosis will be inadequate. In the latter situation reevaluation of the renal vein renin concentrations after correction of stenosis of one renal artery might show that the value is lower on the treated side. This observation would suggest that the residual hypertension was due to persistent disease on the untreated side.

We are not suggesting that the determination of renal vein renin concentrations should supplant renal arteriography or split renal function tests in the evaluation of possible renovascular hypertension. The measurement of plasma renin activity in the effluent blood from both kidneys provides an additional method of ascertaining the functional significance of renal artery stenosis as demonstrated by arteriography. In our experience it

has not always been possible to obtain valid split renal function study data; this has been especially true in the young patient under 5 years of age and in the man over 50 years of age with prostatic enlargement. In these instances renal vein renin assays may be critical in assessing the functional significance of renal artery stenosis. Renal vein blood samples are relatively simple to obtain and entail little trauma to the patient. The major disadvantage of the present renin procedure is that the results are not available for at least three days after the blood samples have been obtained.

In the present study it was found that the determination of plasma renin activity in blood obtained from sites other than the renal veins is often of little value in diagnosis. The inferior vena cava plasma renin activity of patients with subsequently proven renovascular hypertension was frequently within the range observed in patients with essential hypertension or in normal subjects. It is still not known why some patients with correctable renovascular hypertension should be hypertensive if their plasma renin activities are well within the normal range. Regardless of the incompleteness of our understanding of the nature of renovascular hypertension, the data of the present study offer an empirical basis for recommending the measurement of plasma renin activity in both renal veins of the patient suspected of having this disorder.

Summary

Plasma renin activity in the effluent blood from both kidneys has been assayed in a series of 35 patients with hypertension in an attempt to assess its value in predicting the response to corrective renovascular surgery. In 12 out of 13 patients with essential hypertension, the values observed on the left and the right sides were in close agreement with each other; the ratio of the higher value to the lower was 1.4 or less. In 17 out of 18 patients whose hypertension was either cured or distinctly improved by unilateral corrective operations, the preoperative plasma renin activity in effluent blood from the affected side exceeded that of the other side by a factor of 1.5 or more. In two out of three patients who were unimproved by operation, the preoperative plasma renin activity values were comparatively low and were approximately the same for the two sides. In one patient with bilateral renal artery stenosis, the renal effluent plasma renin activity values were symmetrically elevated prior to operation, became characteristic of unilateral renal artery stenosis after corrective surgery on one side, and became normal after corrective surgery on the second side. It is concluded that the determination of plasma renin activity of effluent blood from both kidneys is of potential value in the management of patients with hypertension.

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