A Diagnostic Score Useful for Evaluating the Renogram of Hypertensive Patients[1]

Philip C. Johnson, Jr., M.D. and D. Dwight Odom, M.D.

Houston, Texas

INTRODUCTION

Since 1956, the radioisotope renogram has been presented as a procedure useful in diagnosis of renovascular disease (1-8). However, clinical studies have shown defects in the renogram which could seriously restrict its diagnostic value (9,10). Various modifications and refinements have been suggested to improve the usefulness of the renogram but to date few clinicians would rely on it as the only screening test for evaluating the hypertensive patient.

Several attempts have been made to improve the clinical effectiveness of the renogram by quantitating portions of the curves (8,10-12). A recent article on this subject concluded that "the normal range is sufficiently wide to interfere with the use of the renogram in its present form as a reliable screening test for unilateral renal disease" (10).

Because of the uncertainties encountered when the renogram is used in the diagnosis of renovascular hypertension, we set out to develop a clinical scoring system which could be used to evaluate the renogram. This system was formulated by reviewing the renograms and hospital records of 50 hypertensive patients. Using the clinical scoring system devised from these records, the study was expanded into a review of all renograms performed for hypertensive patients during the last six months of 1962. This review included 183 renograms. The results obtained using the scoring system in the last 79 patients were indentical to those obtained from the first 50 patients used to develop this scoring system. The results were combined therefore, and are the subject of this report.

METHODS

The renograms were recorded using 2 inch diameter sodium iodide scintillation crystals and photomultipliers,[2] ratemeters and a 5 mv dual pen rectilinear servo-recorder.[3] Special detector stands were made for this purpose.[4] The crystals were recessed one inch within 6 inch long and 1 inch thick cylindrical lead shields.[2] The shields were placed against the patient's back with the medial edge of the shields one-half inch from the midline. To insure equal recorder de-

flection for equal dose, the sensitivity of each channel was adjusted prior to each renogram using a standard Cesium-137 source. An integration time constant of 0.05 seconds was used. The recorder paper ran 12 inches per hour. Each pen of the dual pen servo-recorder was set to zero radioactivity at the opposite edge of the paper. On the resulting record, the two curves tend to meet at the center of the paper.

We consider it important to locate exactly each kidney prior to testing. The patient is seated in the special chair shown in Figure 1. A dose approximating 10 μc of I^{131} hippuric acid was injected intravenously with the ratemeters set at a scale factor of 100K and the recorders running. Approximately five minutes later, the detectors were moved up and down the patient's back to locate the area of highest count rate. The detectors were locked over this area. From the height of the tallest test curve, a dose was calculated which would cause the final curve to go exactly half way across the final record. This prevents overlapping of the curves yet produces easily interpreted curves of maximum height. The doses ranged from about 50 to 100 μc of I^{131} with a mean of about 70 μc. The rate-
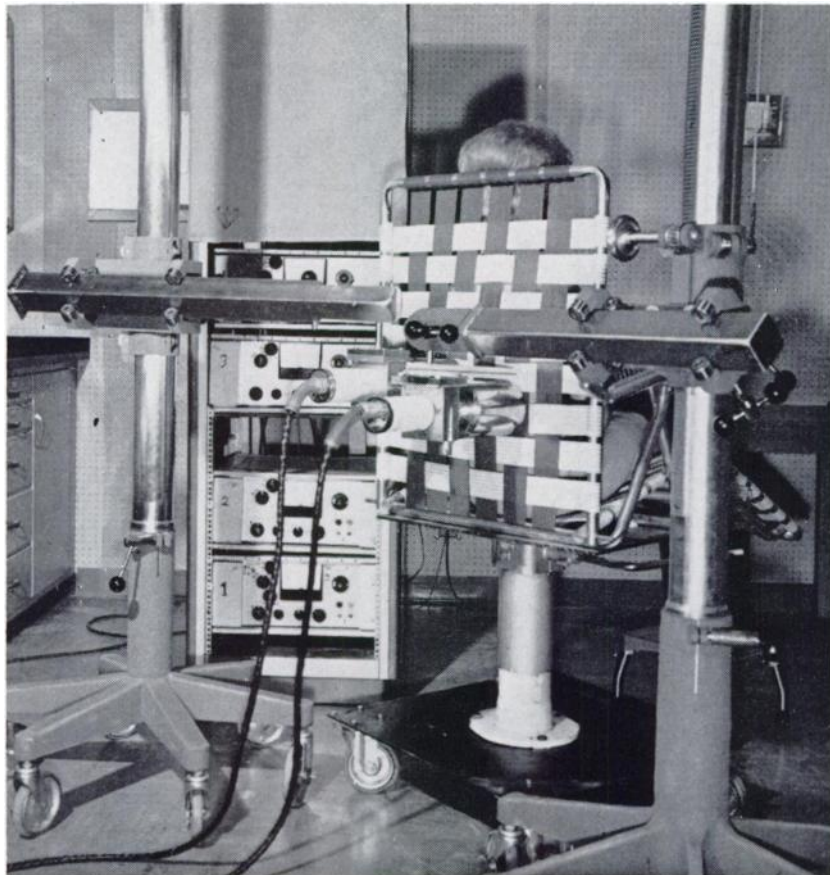

Fig. 1. The chair used for the renogram is a converted lawn chair mounted on a hydrolic lift. The sturdy detector stand allows accurate placement of the detectors and heavy shielding.

meter scale factor was increased to 600 K, each recorded pen was zeroed to the base line at the edge of the paper and the recorders started. The calculated dose was given intravenously taking care to refill with blood the empty syringe as it lay in the vein. This blood was immediately re-injected to complete the injection of the dose. The arm was raised above the head momentarily to prevent the radioactivity from being trapped at the injection site. The curves were recorded until the excretory phase reached 50 per cent of the peak height or for 20 minutes if excretion had not occurred by that time. At the end of the renogram, the detectors were moved to the upper chest area to determine the radioactivity remaining in the blood. The recorder deflection produced by the remaining blood radioactivity is always lower than the values obtained over the kidney. If it is not, it shows a non-functioning or absent kidney.

The state of hydration obviously influences the excretory rate which in turn decreases the time taken for the curve to reach a peak value. The renograms were done without preparation of the patient. However, when a renogram showed borderline results or the curve was too short to allow accurate measurement, the renogram was repeated with the patient having been dehydrated over night. A typical curve is shown in Figure 2. The following measurements were obtained from each renogram curve.

a. Time to Peak: Time from the point when the radioactivity increased to the highest point on the curve.

RENOGRAM

NORMAL HYDRATION

3. 4 MIN.
PEAK
TIME

75%
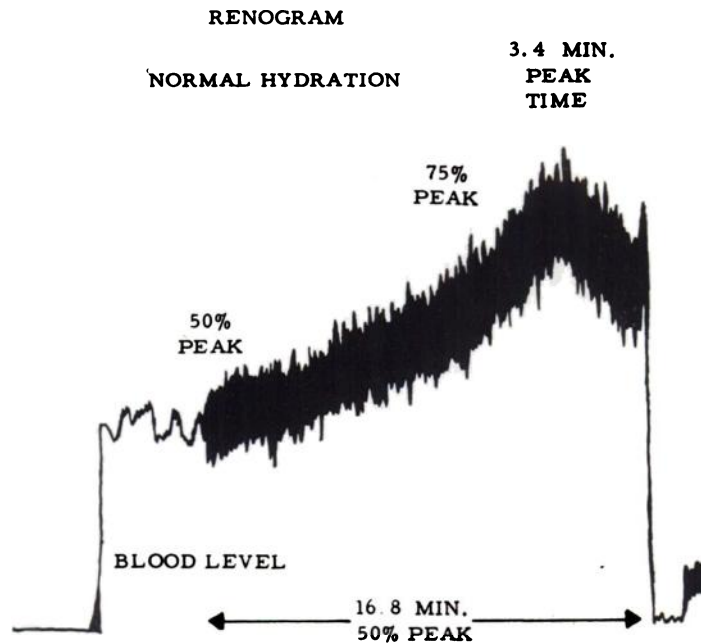PEAK

50%
PEAK

BLOOD LEVEL

16. 8 MIN.
50% PEAK

Fig. 2. This typical curve shows the wide line obtained when one uses a short time constant. Three times: time to peak, time to 75 per cent and 50 per cent of peak height and the height the peak reaches above the base line are recorded as part of the analysis of the renogram. The above curve shows a conspicuous vascular spike.

b. Height: Distance from the baseline to the peak. With the time constants used, the lines drawn by the recorder pens are approximately 0.3 inches wide. The height was measured to the middle of this line.

c. Time to 75 per cent: The time taken for the curve to reach 75 per cent of peak activity, again the mid-point of the renogram line was used.

d. Time to 50 per cent: The time taken for the record to reach 50% of the peak height.

e. Angle: The angle each concentration phase made with the baseline was measured with a protractor.

From each set of values, a ratio was calculated by dividing the value of the left curve by the corresponding value from the right curve. In addition to these ratios, two other features of the curves seemed important and useful in the evaluation of renovascular disease. These were: the vascular spike, which is a monentary sharp increase in radioactivity occurring immediately after injection and shown in the renogram of Figure 2. Its presence shows that the initial level of radioactivity included in and surrounding the kidney or perhaps passing through the kidney is greater than the radioactivity retained within the kidney. A misplaced detector will increase the vascular spike. A second point was failure of either curve to reach 50 per cent of the peak value within 20 minutes.

The renograms used in this study were obtained as part of the diagnostic studies of hypertensive patients. The renograms were performed and reported prior to all other studies and without knowledge of the patient's clinical status or of the results of the other studies. The clinical classification of the patients was made primarily by the vascular surgeons but with the assistance and consultation of the renal section of the Department of Medicine. The final opinion, as written in the discharge summary was taken as the only criteria for classification. Their decision was made from the clinical history and physical examination and the results of routine laboratory studies, arteriograms, intravenous pyelograms, and kidney function tests. Split function studies were performed on those patients in whom renovascular hypertension was strongly suspected by the attending physician. Pressure gradiants across the lesion were invariably measured during surgical repair of the renal arteries and a gradiant of over 15 mm. was considered diagnostic of significant stenosis. The charts of 129 patients who had 183 renograms and 104 arteriograms were reviewed and divided into four catagories: (1) normal, (2) unilateral right renovascular disease, (3) unilateral left renovascular disease, (4) bilateral renovascular disease and (5) bilateral parenchymal disease.

RESULTS

Our results showed that hypertensive patients, free of clinically detectible renovascular disease, had renogram curves which were included in the ranges shown in Table I. We chose hypertensive patients to establish a standard range rather than healthy adults, because it afforded a comparison similar to that confronting a physician in the diagnosis of hypertension. This widens the range, since normal subjects generally excrete the hippuric acid more rapidly, shortening their curves. Analysis of these results did not show a consistent difference between the right and left renogram curve. We have found that the rate of urine

flow changes these ranges. The changes produced by various states of hydration may be compensated for by comparing the two records to each other as a ratio. The range for these ratios are shown in Table I. The greatest difference between the two curves was seen in the concentration angle. The normal range and ratios include at least 65 per cent of the values obtained from curves of the patients free of renovascular disease. Statistical analysis of the normal range was not used because the normal values did not show a normal distribution. This has been noted by others (10).

TABLE I
CRITERIA OF NORMALITY

	Normal Range	Normal Ratios
Minutes to Peak	1.5 — 5.5	0.8—1.2
Minutes to 75%	3.1 — 8.7	0.8—1.2
Minutes to 50%	15.0 —20.0	0.8—1.2
Peak Height		0.7—1.3
Concentration Angle	9.0°—57.0°	0.6—1.4
Vascular Spike		None

From these values, a scoring system was developed. Each ratio not within the set limits was given one point. Each vascular spike seen was given one point, and the failure of either curve to reach 50 per cent of peak value in 20 minutes was given one point. We defined an abnormal renogram as three points or more. Two points was a borderline renogram and one point or less was a normal renogram.

Using the scoring system, the results obtained are shown on Table II.

TABLE II
RESULTS USING NORMALITY CRITERIA

	Number of Renograms	Percent of Renograms
Correct Interpretation	164	89.6
False Positive	5	2.7
False Negative		
Unilateral Stenosis	3	1.6
Bilateral Stenosis	6	3.3
Parenchymal Disease	5	2.7

One-hundred eighty-three renograms were performed. Of these, 164 renograms gave results which correctly diagnosed the clinical problem. Nineteen renograms gave results which were misleading.

When these results were analyzed on the basis of patient's diagnosis, the results shown in Table III were obtained. There were 18 patients in whom incorrect or borderline results were obtained.

We made it a practice to repeat borderline results. Because of borderline renogram results, the test was repeated in 8 of these patients using a different hydration state. In each patient, a correct interpretation could be made from the second renogram. The 11 remaining patients with false positive and false negative

TABLE III

AGREEMENT BETWEEN RENOGRAM AND CLINICAL DIAGNOSIS

	Entire Group	
	No.	*Percent of Total Patients*
Correct Results		
Initial Renogram	110	85.0
Subsequent Renogram	118	91.5
False Positive	4	3.1
False Negative		
Unilateral Stenosis	3	2.3
Bilateral Stenosis	2	1.6
Parenchymal Disease	2	1.6

renograms were not tested again because the renograms were either obviously abnormal or well within normal limits. The false negative results were evenly divided among the various sub-categories.

The percentage of each group who were included in the normal range for each category in the scoring system is shown in Table IV. This Table emphasized several features in the interpretation of the renogram. If we were to use only one ratio for diagnosis, the percentage of false positive and false negative renograms would be greatly increased. As an example, 85 per cent of the ratios of the time to the peak gave values within the normal range when renovascular disease was not present and 36-48 per cent of the curves gave normal values when renovascular disease was present. The 50 per cent excretion value of seventy-four percent of the curves obtained from hypertensive patients without known renovascular disease were within our normal range, still 26 per cent were not. If height only were used, as has been suggested by some, 53 per cent of the renograms from patients with right renal artery lesions would be called normal renograms.

TABLE IV

PERCENT OF HYPERTENSIVE PATIENTS IN NORMAL RANGE

	Other causes of hypertension	*Renovascular disease*		
		Rt.	*Lt.*	*Bilateral*
Number of Patients	63	17	22	27
Curve Criteria		*Percentage*		
Peak	85	36	41	48
75%	87	29	23	30
50%	74	18	4	15
Height	87	53	32	59
Angle	87	47	50	41
Spike	71	35	27	15
All Criteria Combined	94	6	9	7

The percentages within the normal range show similar values for both unilateral and bilateral disease. This suggests that the degree of envolvement in bilateral

disease is usually asymmetrical and it suggests further that the renogram may not be able to separate unilateral from bilateral renovascular disease. It has been our experience that this is true and that we may misinterpret the side of maximum involvement in bilateral disease.

DISCUSSION

Our results show that a renogram can be a highly effective means for evaluating hypertensive patients when the interpretation of the renogram includes a scoring system such as devised here. The method used has several features unlike those of published technics. First, the patient is sitting up rather than lying down. We prefer the sitting position because it simplifies the injection and facilities emptying of the dose from the arm. Our experience has shown that a slow injection obscures the vascular spike. Second, the areas of radioactive concentration are located at the time of the test. In certain patients, the kidneys are highly mobile and we have found kidneys located nearly in the pelvis which were found in the normal position in the routine intravenous pyelogram. Failure to obtain accurate location of the kidney may account for the variability noted by some investigators. Our method eliminates the need for prior x-ray examination of the kidney. Third, a test dose is used rather than a dose related to patient size. This partially eliminates the height of the curves as an absolute index or renal mass or function but it does facilitate measuring the distances on the curves. Fourth, a high counting rate of 300K/minute is used to obtain a better averaging of the radioactive counting rate. We have not found it possible to locate accurately the area of maximum radioactivity using the scale factors of 30K or less because the statistical fluctuation in count rate was great enough to obscure the area of maximum radioactivity.

The importance of precise placement of the renogram detectors can not be overemphasized. We have tested this by using three detectors, one over each kidney with the third detector placed immediately medial, lateral, cephalid or caudad to one of the two kidney detectors. To do this, we have designed a special shield which encloses the two detectors. Their centers were thus only 2 inches apart. Comparisons of the ratio obtained by comparing the curve of this misplaced detector with the curve from the detector centered over the contralateral kidney showed ratios outside of the normal range when the ratio between the two detectors correctly centered over each kidney were within the normal range (13). Similar experience has been reported in the literature (11).

Various technics have been used to locate the kidneys to insure proper placement of the detectors. Winter (16) has cautioned that the detectors must be precisely located over the kidney for a valid test. He and others use a roentgenogram of the abdomen or an intravenous pyelogram to locate the kidneys (5,6,8-12). The kidney is a highly mobile organ which in many patients may move several centimeters with change of position. This has been recognized by at least some authors who specify upright x-ray views for renograms done in the sitting position but neglected by others (4, 9, 12). Whether an x-ray obtained under different conditions and at a different time is an adequate means of locating the kidney has yet to be proven. Nordyke and others have reasoned that

obtaining a preliminary x-ray is time consuming, costly and produces a radiation exposure greater than the renogram (14,15). They have used a blind technic relying on wide angle collimators to preclude the need for accurate location of the kidneys. Wide angle detectors obviously would not have to be positioned accurately. But since they monitor large areas and blood volumes around the kidneys, the initial vascular spike might tend to be more closely related to the surrounding area than of the kidney. Tauxe located the kidneys by determining the point of highest count rate during the early part of the concentration phase (7). In this way, his method is similar to the one used here. However, a misplaced detector ordinarily shows a more prominent vascular spike than that seen when the detector is correctly centered over the kidney area. It is true, also, that a curve from a slightly misplaced detector will show a lower peak concentration than a detector placed over the kidney. Because of these reasons, we have chosen to locate each kidney in a more leisurely fashion during a preliminary test so that artifacts will not be produced by movement of the detectors in the early part of the final record.

Tauxe stated that the most consistent finding in renal artery disease is a delayed excretion, the next most common, the peak height and concentration angle and third, a diminution of the height of the vascular spike (7). Each of these features of the renogram are used in the scoring system used here. Others have stated that small differences in the vascular spike and excretion phase are unimportant when compared to the more sensitive concentration phase (14).

Pircher et al, have listed 28 parameters which could be used to analyze renogram curves (10). They concluded that the peak (maximum) heights, the height of the curves fifteen minutes after injection and the time between the injection and the peak height were the parameters which showed normally distributed values and variances which were not prohibitively large. Ratios such as used in our scoring system were not used, although they did analyze the absolute differences between similar values obtained from the two curves. Our data showed also, large variances and because of this we chose to use ratios of the right and left value rather than the numerical value of differences between the values. A ratio of the values from each curve would tend to correct for variation in hydration state and excretory rate. Using the published results of Pircher et al, obtained from patients with renovascular disease, we calculated ratios similar to those used on our scoring system. When we did this, we found that 8 of the 13 patients had abnormal time to peak ratios. Eleven of the 13 patients with renovascular disease (84%) had two or more ratios beyond our normal range. When the values from the individual renogram curve were compared, only 7 patients had two or more values from either the right or left curve outside of our normal range. This tends to confirm the usefulness of ratios.

The better than 90 per cent correct diagnosis using the scoring system compares to an 80 per cent correct interpretation by Poker et al (9), and 75 per cent correct diagnosis found by others. (8) Using a ratio between the curves rather than absolute values, Block et al, found no false negative results in 15 patients with surgically explored unilateral renal disease and no false negatives among 25 patients without unilateral lesions. These results were superior to that of the Howard Test and the intravenous pyelogram (5). This is different from others

(8,9) who did not use ratios but found other tests of renal function more reliable than the renogram.

Caution should be exercised in comparing the results obtained here with other methods of performing and interpreting the renogram. Many factors other than renographic technic and the method of data analysis might explain the differences in results obtained. Further comparisons must be made before this approach can be considered equal to or superior to that reported by others.

SUMMARY

1. We have presented the values obtained from analysis of renograms performed as part of the diagnostic work-up of hypertensive patients.

2. From these results, a scoring system has been devised which is useful in separating renal artery stenosis from other causes of hypertension.

3. Where this scoring system is used, we obtained 5 per cent false positive and 6 per cent false negative renograms.

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