COMPARISON OF METHODS FOR RENOGRAM EVALUATION

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It is now more than 10 years since the introduction by Taplin (*1*) of the radioisotope renogram as an external measure of unilateral kidney function. Since 1960 ortho-iodohippurate has been available (*2*), and it is generally accepted as the most useful compound for these studies.

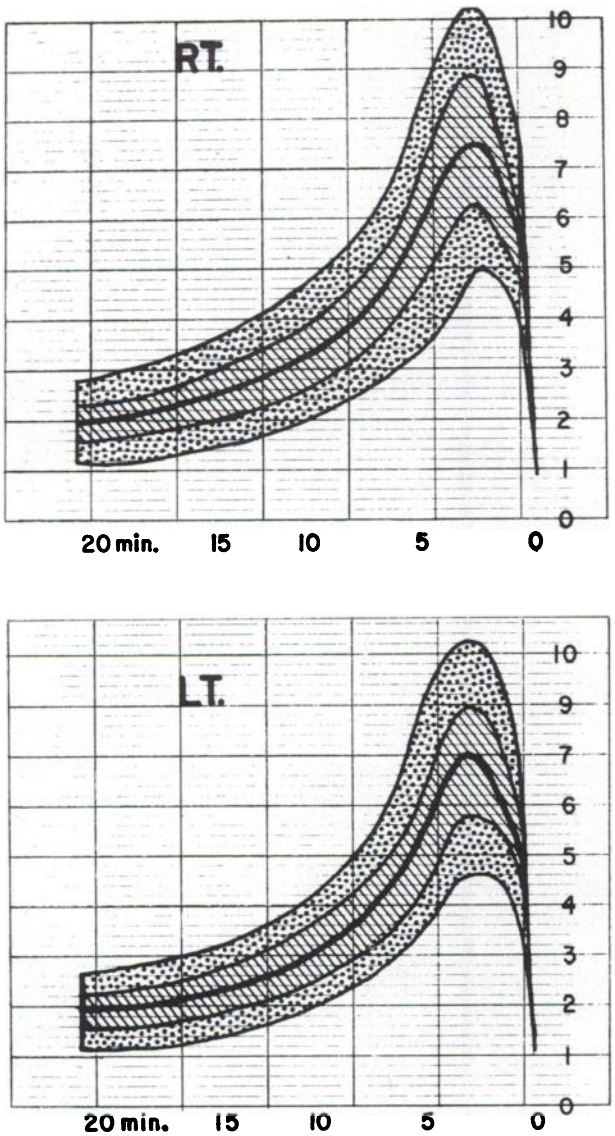

FIG. 1. Range of normal renogram for mean and 1 and 2 standard deviations.

There is little agreement, however, about the most desirable method of obtaining a renogram or the most accurate way of interpreting the result. Most claims about the superiority of one method of patient preparation or the accuracy of a method of interpretation have been made without reference to any baseline normal study used for comparison. In one study—a peak-height comparison of the renogram of the right and left kidney—"patients with only one kidney or with one poorly functioning kidney" were included (*3*).

Our original normal renogram evaluation was based on studies of 78 individuals who were either healthy nonhospitalized young domiciliary members or hospitalized neuropsychiatric patients who were free of hypertension and had no evidence of renal disease (*4*). The results of this study have been the basis of renogram evaluation in this hospital for the past 7 years and have proven reliable for detecting bilateral and unilateral renal disease (*5*). It therefore seemed desirable to use this study to examine the various facets contributing to the renogram in an attempt to gain information about the similarity of the renograms obtained in different laboratories and the relative accuracy of the various parameters used for renogram evaluation. This study was therefore devised to compare: 1. parameters for normal renograms previously obtained in this laboratory with values reported in the literature, and 2. the accuracy of various parameters in separating normal and abnormal renograms.

MATERIALS AND METHODS

The 68 normal renograms used in this study were part of the normal study which has been our basis of renogram evaluation for the past 7 years (*4*). One hundred and four renograms were diagnosed as abnormal either because they fell outside the 2 standard-deviation range of the normal envelope (Fig. 1) or because they deviated upward more than

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2 standard deviations during the first 20 min. Several of the abnormal renograms deviated so far from the usual renogram configuration that many of the parameters could not be calculated: for example, they lacked the secretory or blood-flow rise. Therefore only 42 of the 104 abnormal renograms were chosen for preliminary evaluation. These tracings were chosen because they exhibited the three phases of the normal renogram. The results of this group will be presented separately.

To compare our normal values with those of other authors, studies with similar patient preparation were selected. Our patients were hydrated, seated and the kidney was localized after preliminary isotope injection. All studies were made using a 1½-in. NaI(Tl) crystal and 36-deg collimation using a Picker-Nuclear dual-detector system. In most published methods, adequate equipment description is not available for direct comparison.

A computer program was written to compare 20 parameters for the individual kidney renogram and 11 ratios of one kidney to the other as well as the absolute difference between the two kidneys for five parameters. The mean and standard deviation of each parameter was calculated for the 68 normal renograms. In addition, the 95% range of normal was determined for the absolute difference values. In evaluating the abnormal renograms, the value of each parameter was compared to the 2 standard deviation or the 95% range of normal—whichever was more appropriate—for the parameter. The diagnostic accuracy was defined as the percentage of abnormal renograms in which the parameter fell outside this range. Since cases of unilateral disease were included in the abnormal group, both normal and abnormal individual kidney renograms were evaluated. The accuracy of each parameter in detecting the abnormal renogram was compared to the original renogram evaluation.

The parameters used are shown in Fig. 2. In addition to the ratios indicated, the difference of apparent retention DAR was added (*6*). The ratio is defined as follows:

$DAR = 100 \times (1 - R_1/R_2)$ or $100 \times (1 - R_2/R_1)$ whichever is positive.

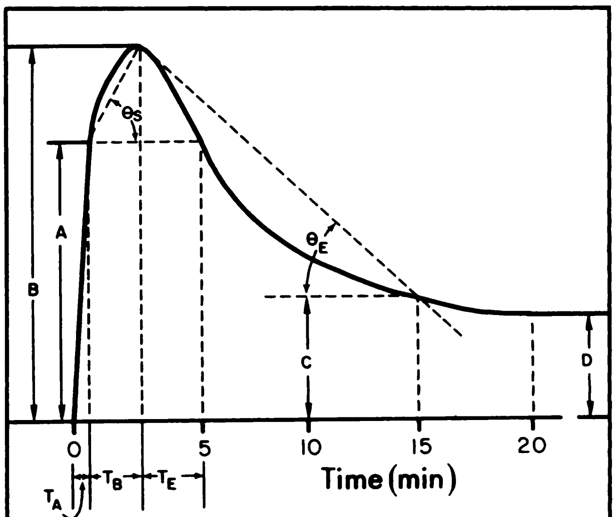
R_1 = Ratio of right to left renogram height at time of earlier peak.

R_2 = Ratio of right to left renogram height 15 min after time of earlier peak.

RESULTS

The mean and standard deviation of the parameters calculated from the normal right and left renograms are shown in Table 1 along with comparable values reported in the literature. There is good agreement for values of time to reach peak and to decline to some fraction of the peak. The agreement is not as good for total concentration, defined as peak height divided by initial height. Because body background is a variable part of initial height, our lower value of total concentration may be due to the wide-angle collimator with its relative increase in background. However, the similarity between our results and those of other authors suggests that renogram results from one institution may be applicable elsewhere.

In a study using methods quite similar to those in our normal renogram evaluation, Tauxe *et al* (*7*) reported normal values of hydrated individuals studied at the Mayo Clinic. Because they reported the mean peak height as 0.72 (times full scale) and we reported it as 3.30 in. in Table 1, we have multiplied our heights by the ratio 0.72/3.30 to allow a



- * 1. Appearance height = A
- * 2. Peak height = B
- 3. Height 5 min after appearance
- * 4. Secretory rise = B − A
- 5. Height 5 min after peak
- 6. Height at 15 min = C
- * 7. Height at 20 min = D
- 8. 20 min height ÷ 5 min height
- 9. Time from injection to appearance = T_A
- *10. Time from appearance to peak = T_B
- 11. Time from peak to return to appearance height = T_E
- 12. Time from injection to 75% of peak
- 13. Time from peak to 50% of peak
- 14. Time from injection to 50% of peak
- *15. Secretory angle = θ_S
- *16. Excretory angle = θ_E
- *17. Total concentration = $(B - A)/A$
- *18. Concentration rate = $(B - A)/AT_B$
- *19. Excretory rate = $(B - A)/AT_E$
- *20. Renogram index = $[(B - A)^2 + (B - C)^2]/B^2$

* Left to right ratios were also calculated for these parameters.

FIG. 2. Parameters used for individual renogram evaluation.

TABLE 1. NORMAL PARAMETERS CALCULATED FROM 68 RENOGRAMS COMPARED WITH PUBLISHED DATA

Parameter	Mean and standard deviation: Wood VA value, Right kidney	Wood VA value, Left kidney	Published data: Value	Published data: Author
Appearance height — A (in.)	2.49 ± 0.49	2.21 ± 0.39	These values are dose dependent and cannot be compared	
Peak height — B (in.)	3.30 ± 0.63	3.05 ± 0.54		
Height 5-min after A (in.)	2.22 ± 0.62	2.08 ± 0.58		
Secretory rise (B — A) (in.)	0.82 ± 0.85	0.85 ± 0.30		
Height 5 min after B (in.)	1.72 ± 0.38	1.60 ± 0.34		
Height at 15 min (in.)	1.04 ± 0.21	1.01 ± 0.21		
Height at 20 min (in.)	0.90 ± 0.17	0.88 ± 0.18		
Height 20 min ÷ height 5 min	0.423 ± 0.090	0.435 ± 0.078		
Time from injection to peak (min)	2.66 ± 0.67	2.75 ± 0.68	2.7	Tauxe (7), Wedeen (8)
			2.4	Brown (9)
Time from peak to return to A (min)	2.25 ± 1.05	2.37 ± 1.15		
Time from injection to return to 75% of peak (min)	5.14 ± 1.08	5.08 ± 1.04	(3.1 to 8.7)	Johnson (10)
Time from peak to 50% of peak (min)	6.14 ± 2.29	6.09 ± 1.95	< 7	Brown (9)
Time from injection to 50% of peak (min)	8.80 ± 2.54	8.83 ± 2.28	< 9	Brown (9)
Secretory angle (deg)	61.6 ± 8.9	60.6 ± 7.7	63	Pircher (11)
Excretory angle (deg)	40.4 ± 7.4	38.2 ± 6.3	49	Pircher (11)
Total concentration	0.337 ± 0.144	0.391 ± 0.150	0.73	Krueger (12)
			0.48*	Tauxe (7)
Concentration rate (min^{-1})	0.167 ± 0.057	0.177 ± 0.062	0.20	Krueger (12)
			0.18*	Tauxe (7)
Excretory rate (min^{-1})	0.160 ± 0.057	0.177 ± 0.054	0.17	Krueger (12)
Renogram index	52.9 ± 9.9	52.6 ± 8.8	62.6 ± 7.1	Hirakawa (13)

* Calculated values.

direct comparison. As can be seen in Table 2, our mean and range of normal values are quite comparable. The differences are believed due, at least in part, to the wider angle collimator used in our study. Tauxe assumes that 27% of the appearance height is background. Our value is 45%. The crystal size is apparently unimportant since we used a 1½-in. crystal and Tauxe uses a 3-in. crystal.

The mean and standard deviation of the ratios and the difference of apparent retention are shown in Table 3. The 2 standard-deviation upper limit of 0.23 for the latter value compares well with the value of 0.20 obtained by Burrows *et al* (*6*). There are no other similarly derived ratios available for comparison. The absolute difference between the two renograms is shown for five parameters in Table 4. As the last column shows, most of the abnormal renograms did not have abnormal differences between the two kidneys.

The diagnostic accuracy of the individual parameters was determined for the 42 abnormal studies which exhibited the three phases of a normal renogram. To illustrate that most of them were not

TABLE 2. COMPARISON OF MAYO CLINIC AND WOOD VA RENOGRAMS STANDARDIZED TO SAME PEAK HEIGHT

Parameter	Mean and range of normal values: Mayo Clinic	Wood VA
Appearance height (in.)	0.50 (0.34 — 0.71)	0.52 (0.34 — 0.70)
Peak height (in.)	0.72 (0.44 — 0.90)	0.72 (0.45 — 0.97)
Peak time (min)	2.7 (1.5 — 4.5)	2.7 (1.3 — 4.0)
Height at 20 min (in.)	0.17 (0.10 — 0.26)	0.21 (0.12 — 0.29)

TABLE 3. RATIO OF LEFT TO RIGHT KIDNEY PARAMETERS

Ratio L/R	Mean and standard deviation	Accuracy in detecting abnormal renograms (%)
Appearance height (in.)	0.900 ± 0.124	28
Peak height (in.)	0.936 ± 0.127	30
Secretory rise (in.)	1.127 ± 0.432	20
Height at 20 min (in.)	0.984 ± 0.120	25
Time from appearance to peak (min)	1.060 ± 0.232	10
Secretory angle (deg)	0.899 ± 0.098	43
Excretory angle (deg)	0.958 ± 0.125	47
Total concentration	1.265 ± 0.481	25
Concentration rate (min^{-1})	1.141 ± 0.409	25
Renogram index	1.005 ± 0.113	50
Difference of apparent retention*	9.5 ± 7.0	10

* See text for method of calculation.

TABLE 4. ABSOLUTE DIFFERENCES BETWEEN NORMAL RENOGRAMS

Difference parameter	Mean difference	95% range	Accuracy in detecting abnormal renograms (%)
Time from injection (min)	0.45	0–1.44	12
Peak height (in)	0.39	0–1.20	5
Height at 15 min (in.)	0.11	0–0.31	21
Height at 20 min (in.)	0.09	0–0.23	29
Secretory rise (in.)	0.23	0–0.52	10

grossly abnormal, the average values for the right renogram in this group are compared to the normal in Fig. 3. Because of unilateral disease, there were eight normal right renograms and seven normal left renograms in this group.

The parameters for each abnormal kidney were compared to the 2 standard-deviation range of normal, and the results are shown in Table 5 in order of increasing diagnostic accuracy. The height of the renogram at any specific time is of little value in separating the normal and abnormal renogram. This was true in spite of rigidly standardized equipment, procedure and dose of isotope. A significant improvement to greater than 70% accuracy is obtained for the last five parameters. These are all derived from the excretory slope or drainage phase of the renogram, and they may all represent variations of the same measurement. However, the diagnostic accuracy appears to increase when the drainage phase is extended to 50% of the peak value instead of only 75%.

TABLE 5. COMPARISON OF PARAMETERS FOR RENOGRAM EVALUATION

Parameter	Accuracy in detecting abnormal renograms (%)
Height—5 min	3
Total concentration (B — A)/A	7*
Height 5 min after peak	13
Secretory rise (B — A)	17
Excretory rate	20*
Height, 20 min	22
Height, 15 min	23
Concentration rate	25*
Time to peak	28
Height, initial	32
Height 20 min ÷ 5 min	44
Secretory angle	44*
Height, peak	49
Time to return to initial height	49
Time to return to 75% of peak	78
Renogram index	89
Excretory angle	91
Time from injection to 50% of peak	93*
Time from peak to 50% of peak	95*

* Normality of distribution is questionable—see text.

The normality of distribution was investigated by calculating an index of skewness (third moment divided by sd^3) and an index of peakedness (fourth moment divided by sd^4). Assuming the acceptable ranges of these indices to be 0 ± 1 and 3 ± 1 respectively (*14*), all but six of the parameters appear to be normally distributed as shown in Table 5. In the cases of time from injection and time from peak to 50% of peak, retrospective examination revealed that one patient's renogram caused this abnormal distribution.

The last five parameters were subsequently evaluated for all of the 104 abnormal renograms. This included 16 normal and 192 abnormal kidney tracings. Each parameter was evaluated for detection of both normal and abnormal renograms. The results are shown in Table 6. Four of the parameters are approximately 90% accurate in detecting both the normal and abnormal renogram. This compares well to the 95% accuracy upon which our original evaluation was based.

TABLE 6. COMPARISON OF FIVE BEST PARAMETERS FOR RENOGRAM EVALUATION

Parameter	Accuracy (%) Normal renogram	Abnormal renogram
Time from injection to 75% of peak	75	78
Excretory angle	87	91
Renogram index	94	89
Time from injection to 50% of peak	87	93
Time from peak to 50% of peak	87	95

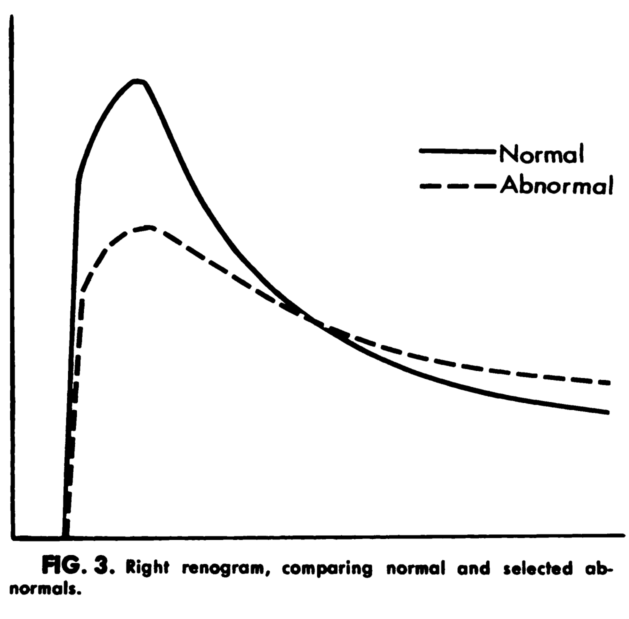


FIG. 3. Right renogram, comparing normal and selected abnormals.

As indicated in Table 3, the ratios were uniformly poor in detecting the abnormal renogram in the 42 selected cases. Likewise, the difference of apparent retention was abnormal in only 10% of the total cases and in one fourth of those with unilateral disease. It should be pointed out that these were not cases of renal artery stenosis for which this parameter was designed.

DISCUSSION

The finding of normal parameter ratios in most of the abnormal renograms is not well understood. This may be due to the fact that two thirds of the 42 selected cases had bilateral disease. Nevertheless, the ratios do not appear to be useful in evaluating the renograms.

The greater diagnostic accuracy of all excretory parameters was somewhat unsuspected. One explanation could have been that the method used to evaluate renograms was weighted toward excretory parameters. Since both the 2 standard-deviation ranges and a change of more than 2 standard deviations in the excretory slope were criteria for abnormality, the excretory parameters would be expected most often to be abnormal if the later criterion was used more often. The renograms were therefore reexamined to see why they were considered abnormal. Seventy percent were outside the 2 standard-deviation range and only 30% were diagnosed as abnormal because of the excretory slope. From this it appeared that our method of evaluation was not weighted toward excretory parameters.

A most probable explanation is that all factors that can produce an abnormal renogram also cause a decrease in the excretory slope. This includes reduction of renal parenchyma and obstruction of urine flow from any cause including increased salt and water retention. This is best illustrated in a mathematical model in Fig. 4 (*15*). Both decreased renal blood flow and prolonged urine transit time prolong the time required to return to a fraction of the peak value.

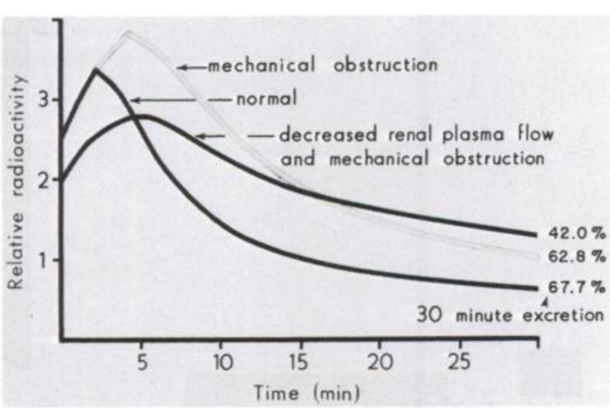


FIG. 4. Delayed excretory phase resulting from either destructive or obstructive disease.

The time from peak to 50% of peak and the time from injection to 50% of peak are equally accurate and appealing because of their simplicity and freedom from necessity for standard conditions. It appears that the dose, sensitivity of equipment, balance of the probes and distance of the kidney from the probe are of little significance. The degree of hydration and position of the patient would, however, effect this value as would the angle of collimation.

These parameters have been further evaluated in a small series of patients all of whom had nephrectomy or renal artery bypass for renal hypertension. In seven who were cured of hypertension following nephrectomy, these two parameters were abnormal on the involved side and normal for the opposite kidney in every case. In five surgical failures, the opposite kidney was abnormal in all but one and the involved kidney was normal in two cases. Admittedly, this is a very small series but the results look promising. Application to a much larger group is needed.

SUMMARY

Sixty-eight normal and 104 abnormal renograms were evaluated according to 19 individual kidney parameters and 11 ratios of one kidney to the other. Good agreement was obtained with normal values of other authors for parameters which were not dose dependent. In general, the greatest diagnostic accuracy was obtained for parameters dealing with the drainage phase of the renogram. The time to return to 50% of peak was 90% accurate in detecting both the normal and abnormal renogram. The ratios were of questionable value in detecting bilateral or unilateral abnormal renograms. The absolute differences between the two kidneys was likewise of little value in detecting abnormal renograms. In the hydrated, seated patient, it appears possible to evaluate accurately the renogram without standardized equipment or dose.

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