Computer-Assisted Static/Dynamic Renal Imaging: A Screening Test for Renovascular Hypertension?

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Computer-assisted static/dynamic renal imaging with [^{197}Hg] chlormerodrin and [^{99m}Tc] pertechnetate was evaluated prospectively as a screening test for renovascular hypertension. Results are reported for 51 patients: 33 with benign essential hypertension and 18 with renovascular hypertension, and for 21 normal controls. All patients underwent renal arteriography. Patients with significant obesity, renal insufficiency, or renoparenchymal disease were excluded from this study. Independent visual analyses of renal gamma images and time-activity transit curves identified 17 of the 18 patients with renovascular hypertension; one study was equivocal. There were five equivocal and three false-positive results in the essential hypertension and normal control groups. The sensitivity of the method was 94% and the specificity 85%. Since the prevalence of the renovascular subset of hypertension is approximately 5%, the predictive value is only 25%. Inclusion of computer-generated data did not improve this result. Accordingly, this method is not recommended as a primary screening test for renovascular hypertension.

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It is estimated that there are some 23 million persons with hypertension in the United States (*1*) and that about 5% of these have renovascular hypertension (*2*). Rapid dynamic renal imaging, alone or combined with static renal imaging, has been proposed as a screening test to detect this subset of hypertensives (*3,4*). Computer-assisted analysis has been claimed to improve diagnostic sensitivity (*5*). At the time this investigation was begun, however, no rigorous assessment of dynamic renal imaging had been performed. We therefore undertook a prospective evaluation of computer-assisted static/dynamic renal imaging in a large hypertensive population and in a normal control group. This procedure was performed on 242 occasions during a 30-mo period ending in 1975. The results are presented here.

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METHODS

Selection of patients. Patients were referred from our Hypertension Center. Those with significant obesity, renal insufficiency, renoparenchymal disease, or hypertension due to other causes (e.g., pheochromocytoma, etc.) were excluded from this analysis, as were patients whose workup was incomplete or in whom the radionuclide studies were technically unsatisfactory. Fifty-one hypertensive patients completed workup that included renal arteriography. In selected patients, plasma renin activity levels in peripheral and renal venous blood were measured. The final classification of hyper-

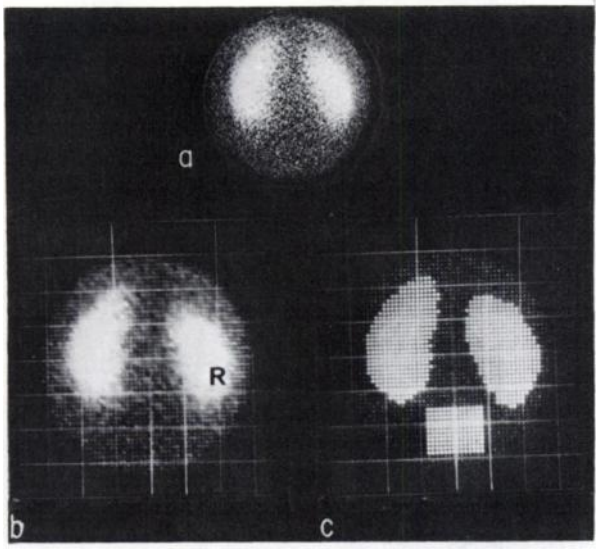

FIG. 1. Normal static renal image. (a) Posterior renal scintiphoto 20 minutes after injection of [^{197}Hg] chlormerodrin. (b) Digital display of static image recalled from tape storage. (c) Flags of both renal outlines and a background region. Renal size and count density were measured from these data.

tension was established by these data.

Normal control group. These were 21 normotensive volunteers aged 20-43 yr, without clinical or historical evidence of renal disease.

Radionuclide imaging technique. There was no preparation. For *static renal imaging* each patient or control subject received 150-200 μCi of [^{197}Hg] chlormerodrin (specific activity 1 mCi/ml) intravenously*. Fifteen to 25 min later the patient was placed prone beneath an Anger camera equipped with spectrometer, low-energy parallel-hole collimator, and video tape recorder linked to a data processor. Both kidneys were centered within the camera field. A static renal image of 40,000 counts was registered and stored.

With the subject's position unchanged and the spectrometer adjusted for detection of Tc-99m photons, *dynamic renal imaging* was performed after rapid (bolus) i.v. injection of 20 mCi pertechnetate (specific activity 25-100 mCi/ml). Data were accumulated on tape at a rate of 100 frames/minute for 1 min and then stored. Maximum count rates fell in the range of 16,000 cps. Variations in field uniformity and size were determined daily with a Co-57 flood source. Studies were excluded if both kidneys did not lie within the camera's field of view. The static image was lost in one patient with renovascular hypertension.

Data obtained. Static scintiphotos of the kidneys (Fig. 1), and sequential dynamic renal images at consecutive timed intervals (Fig. 2A) were obtained. Scintiphotos of 10-20 seconds' duration were also made to improve visualization of the in-

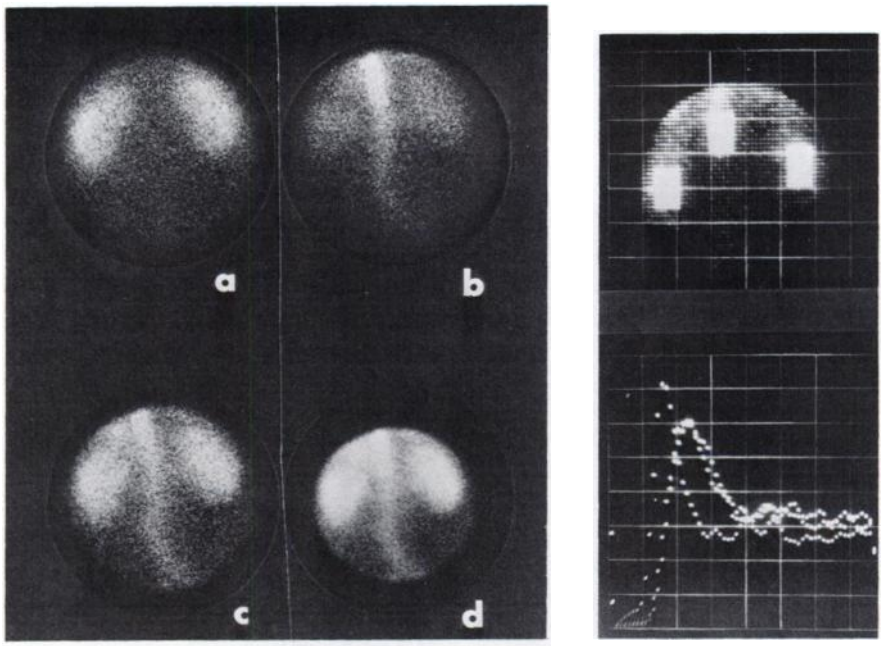

FIG. 2. Normal dynamic renal images and transit curves. (Left) Static scintiphoto (a) locates the kidneys. Arrival of pertechnetate in renal area is demonstrated on selected serial scintiphotos 10-15 secs (b) and 15-20 secs (c) after injection. In this case an integrated image of events between 10 and 26 secs postinjection (d) best demonstrates renal perfusion. (Right) Equal-area renal and aortic flags are shown above. Tracer transit through each region of interest is displayed graphically below. Aortic peak is earliest and highest. Note symmetry of renal transit curves.

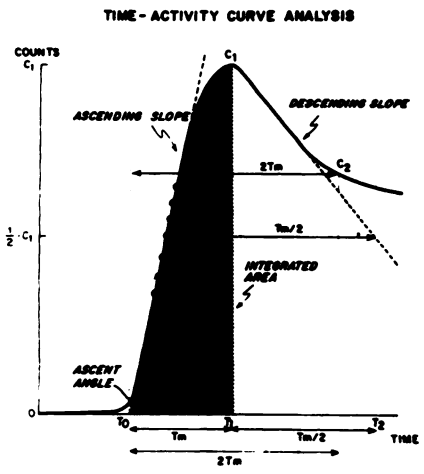

FIG. 3. Numerical analysis of dynamic transit curves. Several measurements shown were evaluated for their sensitivity and specificity.

itial aortic-renal transit of radioactivity (Fig. 2A). These were generated by replay from storage, summing the data on several consecutive frames.

For computer-assisted numerical data analysis, the static renal images were displayed in digital format. There was no correction for attenuation effects due to varying renal depth. The area of each renal image and of a background area were flagged (Fig. 1). The number of matrix units in each renal image (renal size, RS) and the mean number of counts per matrix unit (count density, CD) were determined and corrected for background activity, field nonuniformity, and field size variation. For the dynamic study, equal-sized areas were flagged within the outlines of the kidneys and the upper abdominal aorta (Fig. 2B), and time/activity (transit) curves were generated for each area (Fig. 2B). The initial ascending slopes of the transit curves were determined by fitting a straight line to seven data points centered on and including the half-maximum point, usually encompassing an interval of 4.2 sec (Fig. 3). The ratios of the ascending renal and aortic slopes were calculated (slope ratio, SR).

Several other values (e.g., time to peak amplitude, descending slope ratio, activity at twice peak time, etc.) were also determined from the dynamic transit data (Fig. 3).

Data Analysis. Normal limits for all numerical data were established from results in the control group. Bivariate confidence ellipses, defining the normal ranges with 99.5% probability, were calcu-

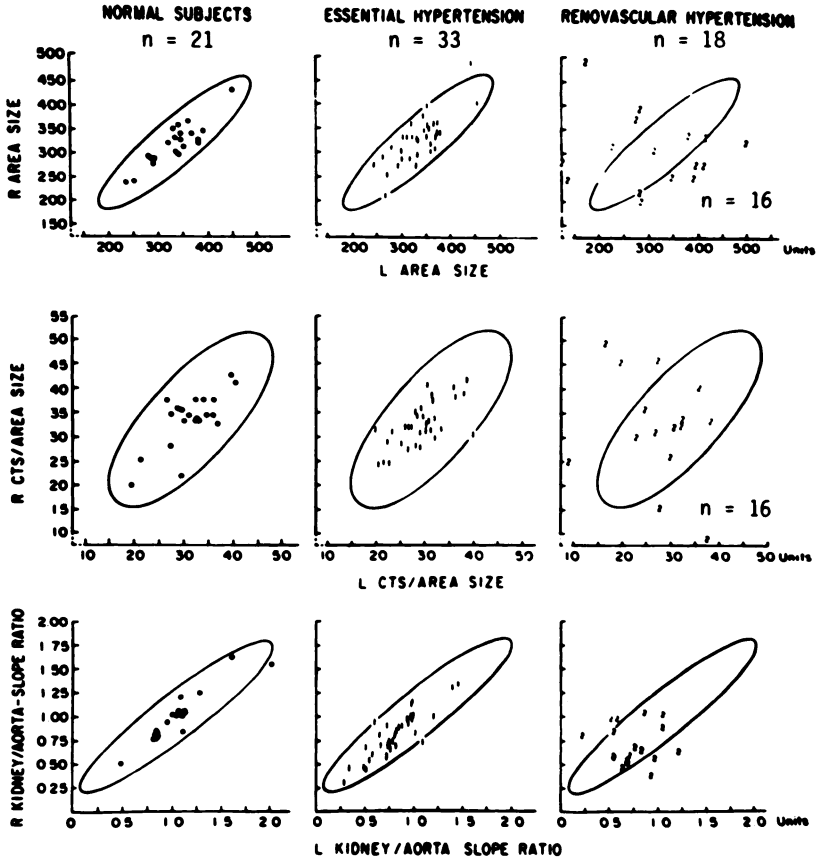

FIG. 4. Variance of major numerical data. Renal size, count density, and slope ratio are shown for normal controls and for patients with benign essential and renovascular hypertension. Bivariate confidence ellipses that define a probability range of 99.5% were calculated from data obtained in normal subjects.

lated for each parameter (Fig. 4) (*6*). Numerical data showing variance ≧3 standard deviations from the mean were classified as abnormal.

The static and dynamic images and transit curves were analyzed independently by two of us (PMJ, LMF), without knowledge of clinical or laboratory data. The analysis considered renal size, symmetry and sharpness of outline, relative intensity of tracer concentration, and symmetry of renal transit curves. An abnormality in the static image, the dynamic images, or the transit curves, alone or together, caused the examination to be classified as abnormal (Fig. 5). In six cases there were minor interobserver interpretive differences that proved unreconcilable at joint review; these were classified as equivocal (see below).

The i.v. pyelograms were interpreted by one observer (DAF) using the criteria of the Cooperative Study of Renovascular Hypertension (*7*).

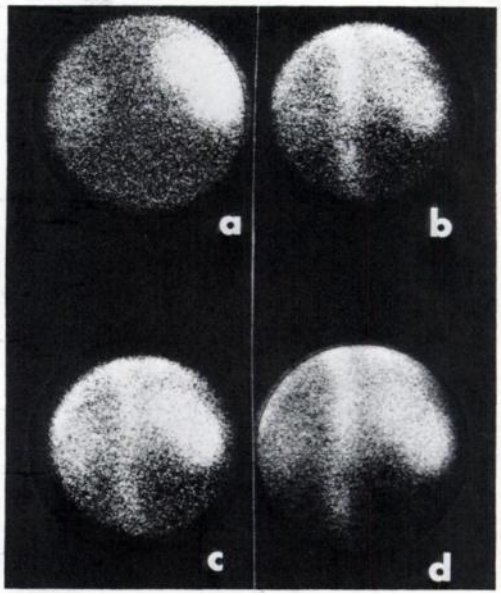

FIG. 5. Renovascular hypertension. All visual data clearly indicate a left renal abnormality. Numerical data and i.v. pyelography were also abnormal in this patient, who had 90% stenosis of left renal artery and significant elevation of renin activity in left renal vein plasma. a) Hg-197 static; b) dynamic 20-25 sec; c) 25-30 sec; d) Σ 17-32 sec.

RESULTS

Fifty-one hypertensive patients met the criteria for this study. Thirty-three had essential hypertension and 18 had renovascular hypertension. Table 1 summarizes their clinical features: those with essential hypertension tended to have a longer history of illness and a lower diastolic blood pressure than those with renovascular hypertension. Of the 18 patients with renovascular hypertension, 13 exhibited cure or improvement of hypertension after corrective surgery, and the other five presented criteria characteristic of the disease based on renin activity levels in peripheral and renal/venous plasma (*8*).

All 33 patients with essential hypertension had normal renal arteriograms. The i.v. pyelogram was normal in 31 patients, falsely-positive in one, and not obtained in one. All 18 patients having renovascular hypertension had abnormal renal arteriograms. The renovascular lesions were due to fibromuscular hyperplasia (n=10), arteriosclerosis (n=6), surgical ligation of the main renal artery (n=1), and narrowing due to renal ptosis (n=1). Fifteen of these patients had abnormal i.v. pyelograms; in three (17%) the examination was falsely negative.

Five patients with renovascular hypertension had bilateral main renal arterial stenoses on arteriography. In four, however, the renal-vein renin data, the intraoperative findings, or the postoperative course indicated that the contralateral stenosis lacked functional significance. The fifth patient had complete occlusion of the left main renal artery and 80% stenosis of the right; there was marked hypersecretion of renin by the left kidney. Hypertension persisted after left nephrectomy but medical management became easier.

Table 2 lists the results of visual data analysis. Of the 18 patients with renovascular hypertension, 17 were correctly identified and lateralized. The

TABLE 1. CLINICAL CHARACTERISTICS

	Age (yr)	Duration (yr)	Highest blood pressure (mm Hg)	Fundi (grade)	BUN (mg/dl)	Serum creatinine (mg/dl)
Essential hypertension	40 ± 11*	6.7 ± 8.2	191 ± 28 / 122 ± 4	I – II	14.7 ± 3.5	1.0 ± 0.2
		$p < 0.05$†	$p < 0.01$†			
Renovascular hypertension	39 ± 13	3.9 ± 6.4	216 ± 37 / 132 ± 19	0 – III	17.2 ± 8.0	1.0 ± 0.3

* Mean ± s.d.
† Wilcoxon's test for unpaired data.

TABLE 2. RESULTS OF INTERPRETATION OF VISUAL DATA* BY TWO INDEPENDENT OBSERVERS

Group No.	Clinical category	Interpretation		
		Negative	Positive	Equivocal†
1	Essential hypertension (n = 33)	27	3	3
2	Renovascular hypertension (n = 18)	0	17	1
3	Control subjects (n = 21)	19	0	2

* Static image, serial dynamic images, and transit curves.

† Indicates unresolvable minor disagreement between interpreters, classed as false positive in Groups 1 & 3, false negative in Group 2.

dynamic images were abnormal in ten, and the static renal images were abnormal in 14 of these patients. The examination was equivocal in one patient (classified as false-negative). In patients having bilateral stenosis of the main renal arteries, a bilateral visual abnormality was observed in only one (Patient 5, above).

In patients with essential hypertension (n=33), visual analysis was normal in 27, equivocal in three, and falsely positive in three. In 21 normal control subjects, visual analysis was normal in 19 but equivocal in two. Equivocal studies in these two groups were classified false positive.

Tables 3 and 4 list results of the major numerical data, RS, CD, and SR. RS was abnormal in 13 patients with renovascular hypertension. CD and SR were less sensitive, as were all other numerical parameters. RS, CD and SR were falsely normal in three patients. In four of the essential-hypertension patients, at least one of these measurements was abnormal. There was poor correlation of visual and numerical data analysis; visual-analysis results were not improved by subsequent inclusion of the numerical data.

Visual data analysis thus exhibited a sensitivity of 94%, a specificity of 85% and, when applied to the general hypertensive population, a predictive value of 25% (Table 5).

TABLE 3. VALUES OF THE MAJOR NUMERICAL DATA IN 21 NORMAL SUBJECTS

Measurement	Left kidney	Right kidney
Renal size, RS (in matrix units)	333 ± 49*	322 ± 44
Count density, CD (counts/unit size)	31.4 ± 5.2	33.9 ± 5.9
Slope ratio, SR (renal:aortic)	1.04 ± 0.31	1.01 ± 0.26

* Mean ± s.d.

TABLE 4. RESULTS OF THE MAJOR NUMERICAL DATA IN 51 HYPERTENSIVE PATIENTS

Type of hypertension		Measurement		
		RS	CD	SR
Essential (n = 33)	normal	31	32	31
	abnormal	2	1	2
Renovascular (n = 18)	normal	3	9	12
	abnormal	13	7	6
	not available	2	2	

DISCUSSION

Intravenous pyelography is the method most widely used to screen for renovascular hypertension. Unfortunately, the appreciable incidence of false-negative and false-positve results makes it an uncertain test (*7,9*).

The present study was undertaken to assess prospectively the efficacy of computer-assisted combined static-dynamic imaging as a rapid screening test for renovascular hypertension. Serial static imaging as performed by Raynaud et al. (*10*) was excluded because it is not a rapid procedure. Recognizing the subjectivity inherent in visual image analysis, we included several quantitative parameters derived from data stored during static and dynamic imaging, establishing their probability ranges in 21 normal control subjects.

Unexpectedly, the sensitivity and specificity of the visual data exceeded those of the numerical data. The variability of the latter limited their predictive value. Data derived from later segments of the renal-transit curves proved unreliable due to the frequency of blunt activity peaks and irregularity of the descending limbs. Transit curves derived from "full kidney" areas of interest were often distorted by nonrenal radioactivity, particularly in the spleen. Since patients with renal insufficiency were excluded, no attempt was made to assess the efficacy of the imaging method in differentiating renovascular and renoparenchymal disease.

The dynamic renal images and transit curves display the initial transit of arterial blood containing pertechnetate. Static [^{197}Hg] chlormerodrin images compare renal tubular function. Visual analysis of these procedures identified 17 of 18 patients with

TABLE 5. DIAGNOSTIC EFFICIENCY OF STATIC/DYNAMIC RENAL IMAGING

$$\text{Sensitivity} = \frac{TP}{TP + FN} = \frac{17}{17 + 1} = 0.94$$

$$\text{Specificity} = \frac{TN}{TN + FP} = \frac{46}{46 + 8} = 0.85$$

$$\text{Accuracy} = \frac{TP + TN}{\text{total}} = \frac{17 + 46}{72} = 0.88$$

Predictive value (Bayes' Theorem) =

$$\frac{\text{(Prevalence)} \times \text{(Sensitivity)}}{\text{(Prevalence)} \times \text{(Sensitivity)} + \text{(1-Prevalence)} \times \text{(1-Specificity)}}$$

For renovascular hypertension:
prevalence = .05 = 5%

sensitivity = .94 = 94%

specificity = .85 = 85%

Predictive value = *25* = *25%*

renovascular hypertension. Four functionally insignificant stenoses of the contralateral main renal artery gave normal visual data. Bilateral visual abnormalities were found in the one patient in whom bilateral stenoses were both functionally significant. This suggests that normal visual imaging data may be evidence that a renal arterial stenosis lacks functional significance.

Although visual analysis was highly sensitive in identifying renovascular hypertensives, six patients (18%) with essential hypertension gave equivocal or false-positive studies. This lack of specificity is compounded by the fact that about 95% of hypertensives do not have renovascular hypertension (*2*). As a result, the predictive value of the method is only 25%, reflecting the low prevalence of this form of hypertension. In reporting a recent study similar to the above, McAfee et al. concluded that rapid dynamic renal imaging should not be used as the primary screening procedure for renovascular hypertension (*11*).

A similar predictive inadequacy has to date obviated all noninvasive screening tests for renovascular hypertension, supporting the recent conclusion that only selected hypertensive patients warrant radionuclide and other specialized diagnostic studies before initiation of antihypertensive therapy (*12, 13*). This position may be short-lived if current radioimmunoassay techniques (*14*) to determine peripheral plasma renin activity levels, and the continuing development of anti-angiotensin II agents (*15*), prove effective.

The low predictive value of combined renal imaging should discourage its use as a primary screening test for renovascular hypertension. Nevertheless, its high sensitivity suggests a possible role in assessing the functional hemodynamic significance of an anatomic renovascular lesion. As refinements in renal imaging and data acquisition occur (*16*), specificity may increase, thereby improving the predictive value of renal imaging as a screening test.

FOOTNOTE

*When this study was undertaken [^{197}Hg] chlormerodrin was the only agent readily available for static renal imaging, and we elected to continue its use throughout the study. Its low photon energy allowed full exclusion of Hg-197 activity during dynamic imaging with Tc-99,.

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