Single-Dose Captopril Scintigraphy in the Diagnosis of Renovascular Hypertension

George N. Sfakianakis, Jacques J. Bourgoignie, David Jaffe, George Kyriakides, Eliseo Perez-Stable, and Robert C. Duncan

Departments of Radiology (Division of Nuclear Medicine), Medicine, Surgery, and Oncology, University of Miami School of Medicine, Miami, Florida

Renal scintigraphy with [^{99m}Tc]diethylenetriaminepentaacetic acid (DTPA) and/or sodium-iodine-131-o-iodohippurate (HIP) was performed before and after an oral dose of captopril (50 mg) in 18 patients with renovascular hypertension (RVH) due to renal artery stenosis (RAS) and 18 controls. In every patient with RVH, captopril induced, enhanced or sustained abnormal findings on HIP scintigraphy depending on the degree of RAS. With DTPA scintigraphy, renal function decreased after captopril in ten kidneys with RVH-related RAS and adequate baseline renal function, but this phenomenon was not evident in 11 kidneys with RVH and poor renal function. Captopril did not influence HIP or DTPA studies of kidneys with patent renal arteries (patients after successful renal angioplasty, patients with essential hypertension, contralateral kidneys of patients with unilateral RVH) or ipsilateral kidneys with mild and subcritical (<60%) RAS in patients without hypertension and/or normal renal vein renin activity. When HIP and DTPA scintigraphy were compared in the same patients, HIP demonstrated greater sensitivity and specificity than DTPA, particularly in patients with poor renal function. HIP scintigraphy before and after a single dose of captopril may provide a rapid sensitive and minimally invasive test for screening patients with hypertension.

J Nucl Med 28:1383–1392, 1987

Numerous tests have been proposed to diagnose renovascular hypertension (RVH). Many have a limited sensitivity or specificity (*1–8*). Suppression of angiotensin II formation by converting enzyme inhibition with captopril or enalapril has recently been used to evaluate RVH by differential renal vein renin studies (*9–12*) or radioisotopic studies (*13–17*).

We compared sodium-^{131}I-o-idohippurate (HIP) and technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) renal scintigraphy before and after a single oral dose of captopril in the investigation of patients with possible RVH. The tests were often performed during a single outpatient visit.

Received Mar. 31, 1986; revision accepted Feb. 23, 1987.

For reprints contact: George N. Sfakianakis, MD, Nuclear Medicine Laboratory (D-57), University of Miami School of Medicine, P.O. Box 016960, Miami, FL 33136.

Parts of this work were presented at the 32nd and 33rd Annual Meetings of the Society of Nuclear Medicine, Houston, TX 1985 and Washington, DC 1986 and were published in abstract form (*J Nucl Med* 1985; 26: P133 and 1986; 27: P961).

METHODS

Renal Scintigraphy

Thirty-six patients suspected of RVH had a baseline and a postcaptopril study. All medications were withheld overnight for both studies and none of the patients received captopril or enalapril treatment for 48 hr prior to the baseline study. In the nuclear medicine laboratory, the patients were hydrated with 10 ml water/kg. Baseline DTPA and HIP scintigraphies were then performed each for 20 min. Three to four hours later on the same day, or on another day, they were given a single oral dose of 50 mg captopril; blood pressure was monitored every 15 min and, 1 hr later (again after hydration), DTPA and HIP scintigraphies were repeated. All four studies were performed in 31 of the 36 patients reported. Pre- and postcaptopril HIP studies only were performed in five patients.

Renal scintigraphy was performed with the patient supine in posterior projection. A large field-of-view gamma camera was used with a general purpose collimator for DTPA and a medium-energy collimator for HIP studies. A dose of 5 mCi (185 MBq) of [^{99m}Tc]DTPA was rapidly injected intravenously. A flow study at 2-sec intervals (1 sec on computer) was obtained for 1 min followed by sequential imaging every 2 min on radiographic film (every 30 sec on a minicomputer)

for 20 min. After bladder emptying, a postvoiding image was obtained. The collimator was changed and the HIP study was performed using 300 μCi (10.1 MBq) of iodine-131 (^{131}I) HIP intravenously. Three minutes later, 40 mg furosemide was injected intravenously (see below). Imaging was obtained at 2 min intervals for 20 min with simultaneous computer acquisition of the data with frames at 30-sec intervals. For both studies, the images on radiographic film were complemented by computer generated time activity graphs of the entire kidneys and of the renal cortices. Slightly modified commercially available software was used (MDS) to define the time of peak activity. Individual kidney function was calculated from the net kidney activity observed at 2 min. The kidney flow curves were analyzed from the peak time of the first pass of the activity and compared to that of the aorta. For the HIP studies alone residual cortical activity at 20 min for each kidney was expressed in percent of the peak cortical activity after background subtraction.

We evaluated the following to interpret the HIP studies: (a) the intensity of the renal cortical activity at 18–20 min as compared to that of the images taken at 2–4 min (visually); (b) the residual cortical activity remaining at 20 min expressed as % of the peak activity (by graph analysis); (c) the shape of the renogram graphs in terms of upslope, peak time and downslope; and (d) the split renal function expressed per kidney as a percent of the net total two kidney counts observed at 1 to 2 min. In normal subjects peak cortical activity occurs at 2 to 5 min with much less cortical activity remaining at 18–20 min than was present at 2–4 min by visual appreciation. Quantitatively <30% of the peak activity remains as cortical residual activity at 20 min.

For the DTPA studies the following analyses were used: (a) the intensity of the renal cortical and collecting system activity for the entire 20 min period; (b) the shape of the time activity graphs in terms of upslope, peak time and downslope; and (c) the split renal function. In normal subjects the kidney cortices and the collecting systems are well visualized and the graph activity peaks at 3–5 min. The DTPA graphs are symmetric in equally sized kidneys in patients with normal renal function. Variations due to hydration are not unusual.

In the flow studies, the peak time of the first-pass time-activity graph was compared with that of the aorta. In normal kidneys the first-pass activity peak usually follows the aortic peak by a few seconds.

Effective renal plasma flow (ERPF) was measured using the regression analysis of Tauxe from a single blood sample obtained at 44 min (*18*). In some patients, GFR was measured using the DTPA renal uptake analysis of Gates (*19*).

The resolution of the HIP renography is limited by septal penetration of the high-energy photons of ^{131}I (364 keV). To separate cortical and collecting system activities, as much as possible, continuous accumulation of the radionuclide in the collecting system was prevented by a diuresis induced with 40 mg furosemide administered intravenously 3 min after the injection of HIP. Most patients received furosemide after completion of the DTPA study at the beginning of HIP study.

Population Studied

A final clinical diagnosis was reached in 36 patients by angiography and split renal vein renin measurements, or follow-up measurements of blood pressure after angioplasty. Eighteen patients found to have RVH and 18 control subjects are reported here.

The control group included: (a) seven normotensive subjects including one with abdominal aneurysm, one with Takayasu's disease and mild bilateral renal artery stenosis, and two patients who had undergone renal transluminal angioplasty for RVH and remained normotensive without antihypertensive medication; (b) 11 hypertensive patients, with intact renal arteries on angiography.

The group of patients with RVH included: (a) ten hypertensive patients with unilateral RAS (nine main, one branch; (b) six hypertensive patients with bilateral RAS, (five with bilateral main RAS and one with a branch stenosis on one side); and (c) two hypertensive patients with a single transplanted and functional kidney and RAS (one main, one branch).

RVH was diagnosed by renal vein renin measurements using the lateralizing criteria of Vaughan et al. (*20*) and/or by the therapeutic benefit of angioplasty. Angiography (Table 1) in the 18 patients with RVH showed 21 kidneys with high grade and three with complete renal artery (RA) obstruction. Arbitrarily, RVH kidneys were separated in the following categories: complete (100%) RAS (three kidneys), nearly complete (>95%) RAS (five kidneys), severe (60–95%) RAS (16 kidneys). All had increased ipsilateral renal vein renin activity or responded to angioplasty.

Kidneys not causing RVH included the contralateral kidneys of patients with unilateral RVH and both kidneys in patients without RVH. Twenty-nine kidneys had normal angiograms and nine had mild and insignificant (<60%) RAS of which four were found in normotensive patients. All nine had normal renal vein renin activity. In addition, this group included six kidneys from control normotensive individuals not subjected to angiography. Finally the normal portions (with normal branches of renal arteries) of three kidneys with branch RAS were also counted in this group.

RESULTS

Data is summarized in Table 1. Baseline HIP studies were abnormal in eight of 24 RVH-related kidneys; three did not visualize angiographically or isotopically (100% RAS) and five small and hypofunctioning kidneys with nearly complete (>95% RAS) obstruction visualized late on renography with a characteristic pattern of continuously increasing isotopic activity. All eight had ipsilateral lateralizing renal vein renin studies. Captopril had little or no effect on the HIP studies of these kidneys.

In contrast, baseline HIP renography was normal with a residual cortical HIP activity <30% of the peak activity in 16 of 24 kidneys causing RVH. Nine had a normal and seven had a reduced function as assessed by ERPF. Captopril increased the 20 min residual cortical HIP activity to more than 40% of the peak activity in all 16 kidneys and, in most cases, changed the renogram characteristically from a curve peaking early into one which either reached a plateau or did not

TABLE 1
Correlation Between Angiography, Renal Function, and Scintigraphy

Angiography	Number of kidneys	Renal function*	Scintigraphy			
			[^{131}I]hippuran		[^{99m}Tc]DTPA	
			Baseline	Captopril	Baseline	Captopril
A. RVH-related kidneys						
1. Complete (100%) RAS	3	None (3)	Non vis	Non vis	↓↓ (3)	Unchanged
2. Nearly complete (>95%) RAS	5	↓↓ (5)	+	Unchanged	↓↓ (4)	Unchanged
3. Severe (60–95%) RAS	16	N (9)	N	+	N (7)	↓
		↓ (7)	N	+	↓ (3)	↓↓
					↓ (4)	Unchanged
	24	(24)			(21)	
B. Kidneys not causing RVH						
1. Mild (<60%) RAS	9	N (9)	N	Unchanged	N (5)	Unchanged
2. Normal arteries†	38	N (28)	N	Unchanged	N (24)	Unchanged
		↓ (6)	P	Unchanged	↓ (5)	Unchanged
		↓↓ (4)	P	Unchanged	↓↓ (4)	Unchanged
	47	(47)			(40)	

* Decrease in renal function assessed by split ERPF or GFR (DTPA analysis or creatinine clearance) (↓ <80% decrease; ↓↓ >80% decrease).

† Includes six kidneys without angiography in normotensive controls (see text).

Abbreviations: RVH: Renovascular hypertension; RAS = Renal artery stenosis; N = Normal; non vis = nonvisualization; + Typical RVH curve (see Figs. 1 and 4); P = Plateauing curve of kidney with intrinsic renal disease (see Fig. 4).

peak within 20 min. This prolongation by captopril of the cortical transit of HIP was evident in patients with either normal or decreased renal function; it was evident on the images and on the graphs of patients with RVH secondary to main RAS (Fig. 1A) or branch artery stenosis (Fig. 2).

Baseline HIP studies were normal in nine kidneys with mild and subcritical (<60%) RAS. Captopril had no effect on the HIP images or renograms of these kidneys. Included in this group are two normotensive patients with bilateral subcritical RAS (Fig. 3A) and five patients with RVH caused by the contralateral kidney and normal renal vein renins ipsilaterally. Captopril also had no effect on the HIP study of 38 kidneys without RAS, of which 28 had a normal baseline study and ten (with decreased ERPF) showed baseline renogram characteristics of intrinsic renal disease. It was not difficult to differentiate these ten kidneys with intrinsic disease, in which the HIP renogram remained flat, from RVH-related poorly functioning kidneys with severe RAS, in which HIP activity slowly accumulates in an ascending renographic curve (Fig. 4).

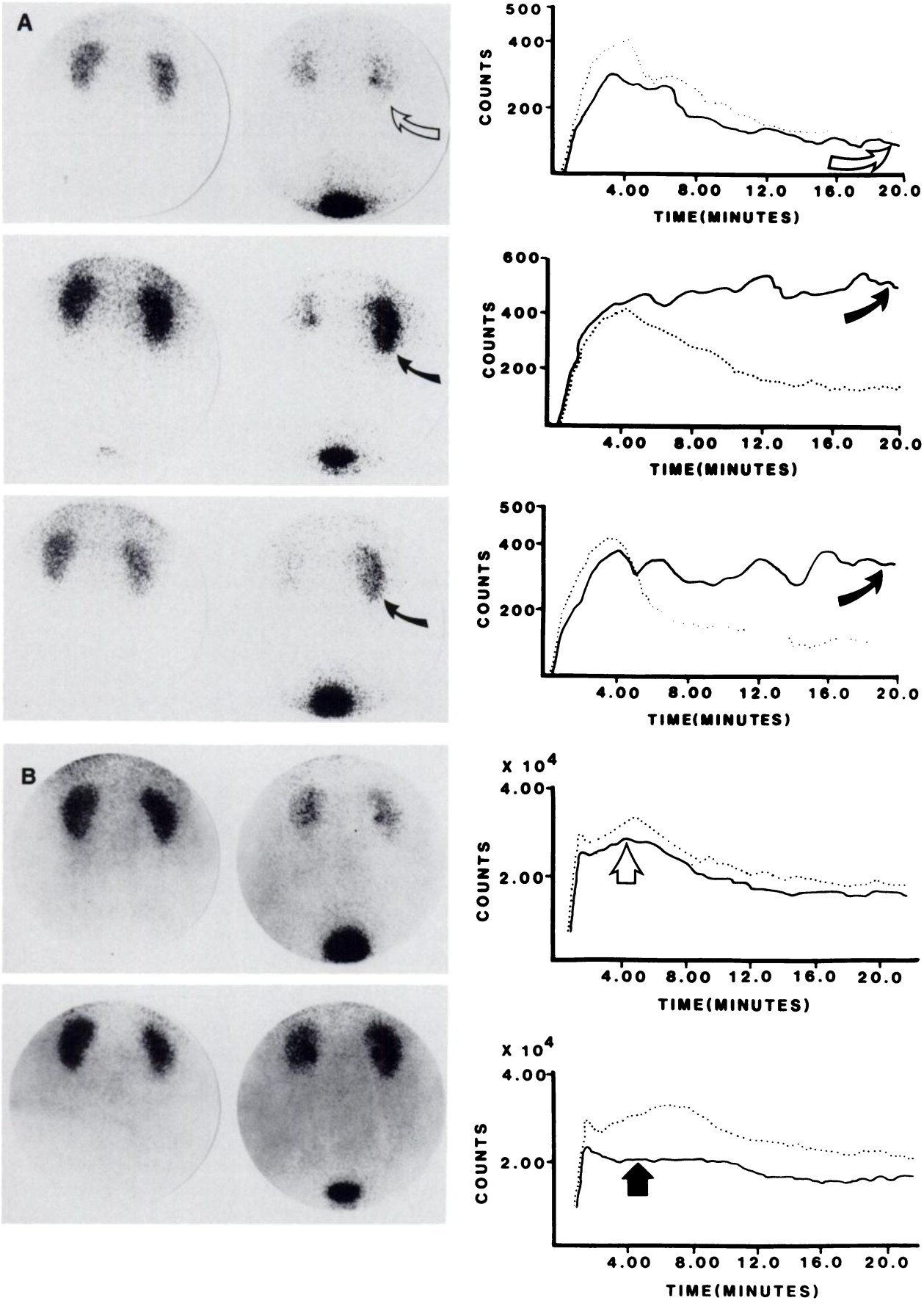
To evaluate the effect of furosemide, ten HIP studies were performed with and without furosemide in five patients with RVH and in five patients without RVH. The use of furosemide did not change the results of the studies but delineated more clearly the true cortical activity by preventing accumulation of HIP in the collecting system (Figs. 1 and 3), thus avoiding false interpretations.

Baseline renal flow studies did not consistently distinguish between normal kidneys and kidneys with RAS causing RVH. Captopril did not induce a deterioration in the images or in the flow graphs in either group. As a matter of fact, an improvement in flow was occasionally evident in kidneys with or without RVH after captopril.

Baseline DTPA studies were abnormal in seven kidneys with complete or greater than 95% RAS; like HIP, the images and curves of DTPA studies remained unchanged in these instances.

In contrast, in RVH kidneys with a severe (60–95%) RAS and a normal baseline function, captopril induced a dramatic decrease in renal cortical DTPA activity which was best appreciated between 6–20 min after injection. However, when baseline function was reduced in RVH-related kidneys as assessed by ERPF, a decrease in the renal accumulation (filtration) of DTPA was not always evident by visual appreciation of the scintigrams (Fig. 1B). Thus only seven of 14 RVH kidneys with severe (60–95%) RAS demonstrated a visible decrease in DTPA activity after captopril, including two kidneys with branch stenosis (Fig. 3). The time-activity graphs clearly showed the suppression of filtration when baseline function was normal and were a more sensitive index of captopril-induced decrease in filtration than the images, providing such evidence in an additional three kidneys with a mild decrease in renal function (Fig. 1B), thus improving the detectability of RVH to ten of 14 kidneys with severe (60–95%) RAS.

Captopril had no effect on DTPA studies in seven kidneys with subcritical RAS (<60%) and in 24 kidneys with normal arteries and normal baseline renal func-


A
B
500
400
200
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)
600
400
200
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)
500
400
200
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)
X 10^4
4.00
2.00
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)
X 10^4
4.00
2.00
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)

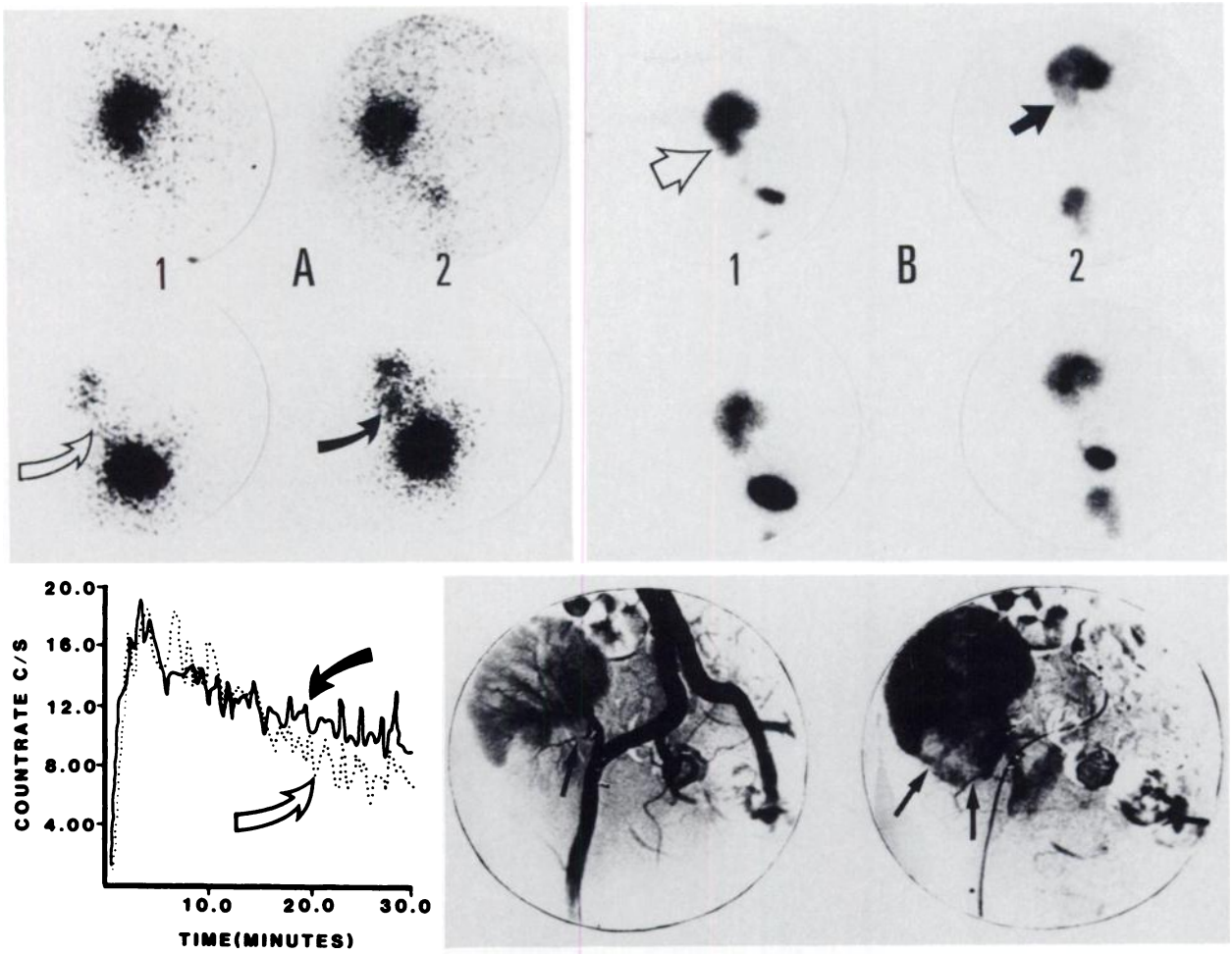


FIGURE 2
Angiography of a transplanted kidney in a 55-yr-old man who developed acute hypertension showed a severe stenosis of a branch artery (arrow, left image) with delayed nephrogram of the lower pole of the kidney (right image), HIP (A) and DTPA (B) images at 4 min (top) and 20 min (middle) without (1) and with captopril (2) are shown. In comparison with baseline studies, captopril enhanced HIP retention and decreased DTPA image in kidney's lower pole (arrows). Residual cortical activity of HIP at 20 min for the entire kidney was 30% without captopril and 50% after captopril (arrow). ERPF was 140 and 129 ml/min 1.73 m^2, respectively.

tion. Similarly abnormal baseline DTPA studies in nine kidneys with normal renal arteries but renal insufficiency remained unchanged after captopril (Fig. 4). These nine kidneys without RAS but with intrinsic disease could not be easily differentiated from RVH-related kidneys with RAS and compromized function using DTPA studies (Fig. 4).

STATISTICAL ANALYSIS

Two approaches were followed for the analysis of the data, using the effect of captopril alone or the effect of captopril in association with other criteria (Table 2).

1. When the deteriorating effect of captopril on scintigraphy was used as the sole criterion for RVH, the

FIGURE 1
A: Data in a 51-yr-old man with hypertension and a 70–80% stenosis of the right renal artery. Blood pressure was 184/90, 116/68, and 134/78 mmHg and ERPF was 316, 244, and 216 ml/min. 1.73 m^2 before, after captopril and after captopril plus furosemide, respectively. HIP images at 4 min (left) and 20 min (right) and graphs do not indicate RVH before captopril (upper). Captopril without (middle) or with furosemide (lower) induced changes typical of RVH in the right kidney (continuous line, arrows). Cortical residual activity at 20 min increased from less than 30% to 100% of the peak activity. Split renal function was 46%/54% (R/L baseline) and became 41%/59% (after captopril). B: DTPA images (4 min left, 20 min right) and graphs were symmetric before captopril (upper). After captopril (lower), the DTPA images are little modified but the DTPA curve shows a decrease in right kidney function (arrow) by 7% of the total renal function. Renal blood flow images and curves (not illustrated) showed only a slight decrease in right kidney perfusion compared to the left kidney before captopril and little change after captopril. Posterior views, continuous line, right kidney; intermittent line, left kidney.

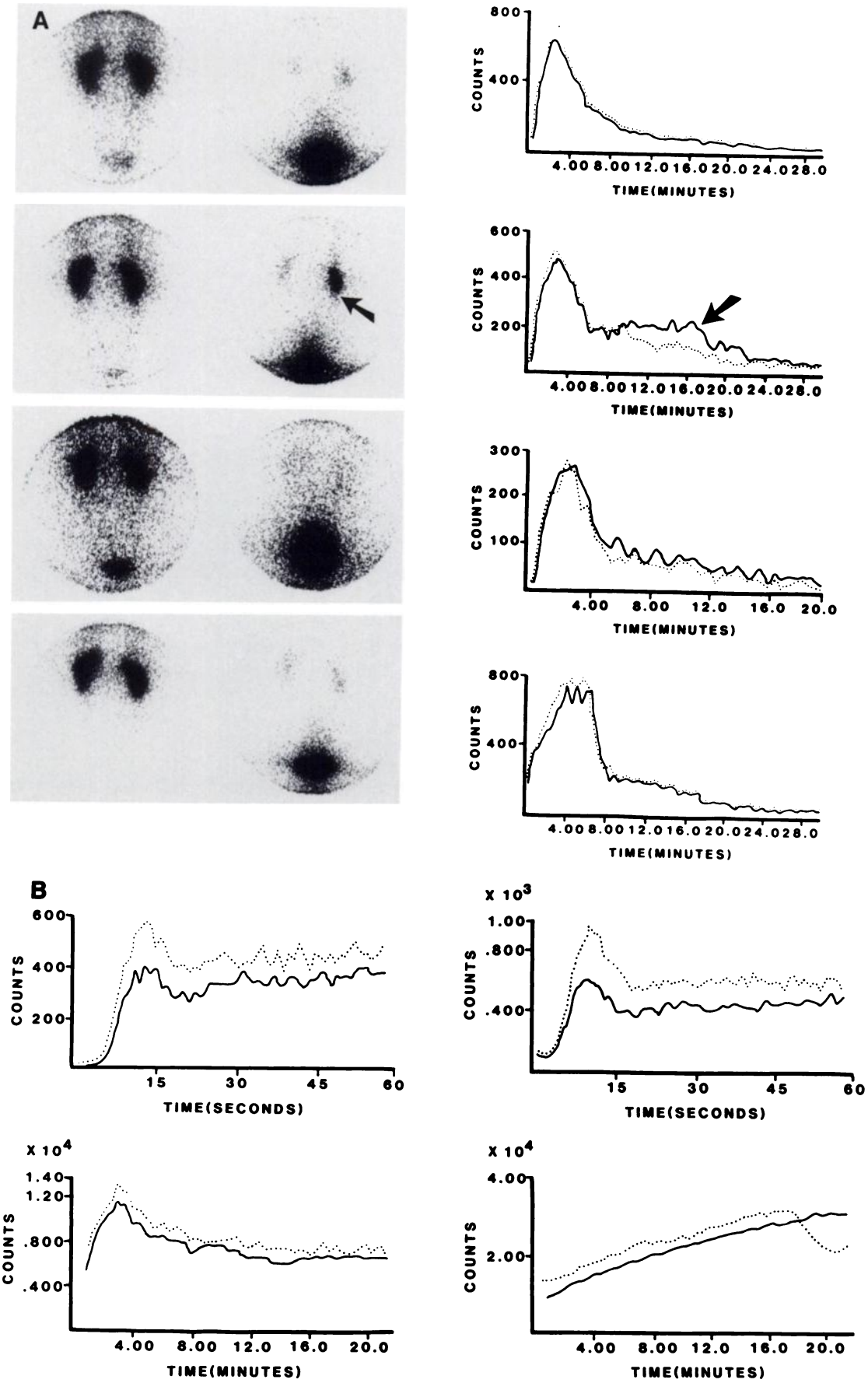

A
800
400
COUNTS
4.00 8.00 12.0 16.0 20.0 24.0 28.0
TIME(MINUTES)
600
400
200
COUNTS
4.00 8.00 12.0 16.0 20.0 24.0 28.0
TIME(MINUTES)
300
200
100
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)
800
400
COUNTS
4.00 8.00 12.0 16.0 20.0 24.0 28.0
TIME(MINUTES)
B
600
400
200
COUNTS
15 30 45 60
TIME(SECONDS)
X 10^3
1.00
.800
.400
COUNTS
15 30 45 60
TIME(SECONDS)
X 10^4
1.40
1.20
.800
.400
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)
X 10^4
4.00
2.00
COUNTS
4.00 8.00 12.0 16.0 20.0
TIME(MINUTES)

FIGURE 3

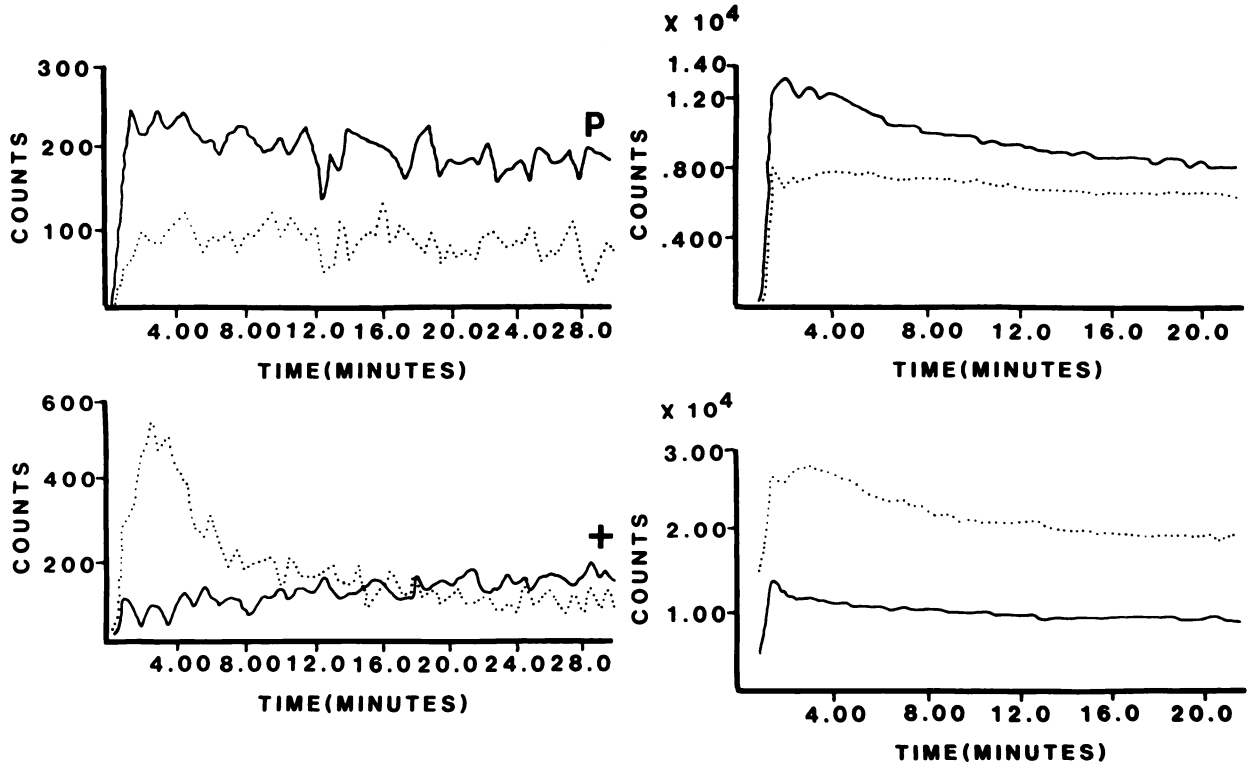


FIGURE 4
Upper panels: data from a 82-yr-old man with azotemia, patent renal arteries and essential hypertension. HIP (left) and DTPA (right) curves show better function in right than in left kidney, but flat curves indicate poor function bilaterally. Captopril had no effect on either study (not illustrated). BP and ERPF were 180/110 mmHg and 80 ml/min. 1.73 m^2 before and 135/80 and 93 ml/min. 1.73 m^2 after captopril, respectively. Lower panels: data from a 66-yr-old man with nearly complete (>95%) stenosis of the right renal artery and renovascular hypertension. HIP (left) and DTPA (right) curves have normal shape for the left kidney but show severe reduction in function of the right kidney. Captopril had no effect on either HIP or DTPA. However, HIP study in this patient shows slowly increasing HIP activity in the right cortex suggesting RVH. DTPA studies in the two patients appear alike. BP and ERPF were 180/90 mmHg and 144 ml/min. 1.73 m^2 before and 150/85 mmHg and 190 ml/min. 1.73 m^2 after captopril, respectively. Continuous lines, right kidneys; intermittent lines, left kidneys.

specificity of both tests was high (100%) but the sensitivity was 67% for HIP and 48% for DTPA.

2. When nonfunctioning kidneys and those with an abnormal baseline HIP study characteristic of RVH and the corresponding abnormalities on DTPA were included as additional criteria, the sensitivity of both tests was high (100%) but the specificity of DTPA was 73%, whereas that of HIP remained at 100%. Although a cross-sectional study of this nature provides only provisional estimates of sensitivity and specificity, HIP appears to be better test under both approaches. Using the McNemar test (*21*) we found that (a) employing the deteriorating effect of captopril a sole criterion for comparison and the continuity correction factor, the differences between DTPA and HIP are not statistically different ($X^2 = 2.25$); without the continuity correction, DTPA and HIP results are significantly different ($X^2 = 4.00$; $p < 0.05$); (b) including the additional criteria

FIGURE 3
A: HIP images and graphs in a 25-yr-old woman with Takayashu's arteritis, bilateral mild (<60%) renal artery stenoses and normal renal vein renin studies. HIP images at 4 and 20 min and renograms were normal before captopril (upper study). Retention of HIP after captopril (second study) was of concern (arrow). Studies repeated with furosemide (third study) and with captopril plus furosemide (lower study) showed normal and identical images and curves in both kidneys suggesting that the retention of the isotope in the prior study resulted from inadequate emptying of the urinary collecting system. B: DTPA flow studies (upper) and DTPA renograms (lower), baseline (left) and post captopril (right). Flow study remained normal after captopril (upper right). Baseline DTPA study (lower left) was normal but confusing after captopril (lower right), because of decreased urine production. BP was 160/90 before and 150/80 after captopril; and 160/90 with furosemide alone and 135/90 with furosemide plus captopril. Concomitant ERPF values were 551, 709, 539, and 661 ml/min. 1.73 m^2, respectively. Since this study, the patient has remained normotensive without antihypertensive medication for over 1 yr.

TABLE 2
Statistical Comparison of HIP and DTPA Studies in Kidneys with RVH and in Control Kidneys

	Captopril effect alone*		Captopril effect plus other criteria*	
	HIP	DTPA	HIP	DTPA
RVH (N = 21)				
Positive	14	10	21	21
Negative	7	11	0	0
Control (N = 40)				
Positive	0	0	0	11
Negative	40	40	40	29
Specificity, %	100	100	100‡	73‡
Sensitivity, %	67†	48†	100	100

* See text.
† $X^2 = 4.00$ ($p < 0.05$).
‡ $X^2 = 35.5$ ($p < 0.001$).

cited above the differences between DTPA and HIP are highly significant (corrected $X^2 = 35.5$, $p < 0.001$).

DISCUSSION

Differential renal vein renin measurements are now standard for diagnosing and lateralizing RVH with a diagnostic sensitivity of 74% and a specificity of 100% (*8*). Converting enzyme inhibition with captopril or enalapril further enhances the accuracy of the test (*9–12*). However, the procedure remains invasive requiring catheterization of the vena cava and renal veins. The sensitivity is high but it usually takes several days for the results to be returned. Transluminal angioplasty performed on angiographic criteria alone is empiric treatment at best.

In patients with RVH, converting enzyme inhibition reduces iodine-125 (^{125}I) thalamate extraction in the kidney with a stenotic artery but not in the contralateral kidney with an intact renal artery (*13*). Captopril also has little effect in kidneys of patients with essential hypertension. Similar observations were made with HIP. In patients with RVH, Wenting et al. (*13*) found a 70% decrease in [^{125}I]thalamate extraction and a 50% decrease in HIP extraction. Captopril dramatically reduced the uptake of DTPA (*13–15*) or [^{99m}Tc]dimercaptosuccinic acid (DMSA) (*16*) in the kidney beyond the arterial stenosis. Similar findings were reported in patients after a single oral dose of 25 mg captopril in whom a DTPA scintigram was repeated several days after a baseline study. In that setting, HIP showed a "less pronounced decrease in radiopharmaceutical concentration" (*17*). Most importantly, arterioplasty cured the hypertension of all patients with scintigraphic evidence of captopril-induced suppression of function in the affected kidney (*13*).

The data reported here indicated that one 50 mg oral dose of captopril was partially successful in diagnosing RVH based on the deteriorating effect of the drug on the renal images and the time activity graphs generated by DTPA and HIP scintigraphy, with a specificity on the order of 100%. It was evident that at least two parameters played a major role in the sensitivity of the single dose captopril scintigraphy, namely the degree of stenosis of the RA and the overall functional integrity of the RVH-related kidney. The degree of the RAS has, obviously, a continuous spectrum ranging from an asymptomatic mild stenosis, <60% of the lumen, through RVH-related moderate and severe RAS, to a 100% RAS, the angiographic "complete obstruction". Similarly, renal function ranges from normal to renal failure. The separation of the kidneys in groups with 100%, more than 95%, 60–95% and 40–60% RAS, or in groups with normal, decreased function or renal failure, might eventually prove to be not entirely proper, when more studies have been performed. In this preliminary report, however, this grouping seemed reasonable on the basis of the clinical presentation, the specific findings on scintigraphy, renal vein renin measurements and angiography and, finally, because of the outcome of the angioplasty in some patients who had this therapy.

Only eight of the 24 RVH-related kidneys in this series had abnormal baseline HIP studies and 14 had abnormal, but not characteristic, DTPA studies. Thus, this report confirms the limited sensitivity of renal scintigraphy in diagnosing RVH (*6*). On the other hand, the data indicate the usefulness of a single oral dose of captopril to increase the sensitivity and the specificity of both DTPA and HIP tests to diagnose RVH on the basis of the deteriorating effect of the drug on scintigraphy.

It is easy to understand why captopril increases the sensitivity of DTPA scintigraphy in the diagnosis of RVH. DTPA is a glomerular filtrate marker (*22*). RVH is a condition where GFR in the ipsilateral kidney is angiotensin II dependent (*23,24*). By preventing local angiotensin II formation, captopril decreases GFR and the renal excretion of DTPA. On the other hand, the renal excretion of HIP is governed mainly by proximal tubular secretion and to a lesser extent by glomerular filtration. As captopril decreases filtration and filtration fraction in RVH kidneys, the availability of HIP for tubular uptake and secretion increases. The tubules accumulate HIP but, as the urine flow decreases, the activity in the cortex accumulates. The lack of effect of captopril on renal blood flow in RVH-kidneys has also been reported in animals (*25*) and can be explained by the resulting postglomerular vasodilation. The latter decreases intraglomerular pressures and glomerular filtration but facilitates blood flow through the glomeruli. Whether blood flow remains constant or even increases

after captopril may depend on the concomitant effect of the drug on systemic and renal arterial pressure. These effects of captopril are confined to the ipsilateral kidney in RVH where glomerular hemodynamics are angiotensin-II dependent. The latter is not the case in the contralateral kidney or in kidneys with normal arteries or with subcritical RAS. Captopril does not change glomerular hemodynamics and, therefore, has no effect on DTPA or HIP scintigraphies in these kidneys.

In our group of patients HIP scintigraphy was more useful than DTPA. The findings with both tests in the same patients can be summarized as follows.

1. As expected, neither HIP nor DTPA showed any effect of captopril on three kidneys with angiographically "complete obstruction" of the RA, although these kidneys were producing high renin activities. HIP did not even visualize these kidneys and DTPA barely showed a blood-pool activity.

2. Neither HIP nor DTPA demonstrated a captopril effect on four RVH kidneys with nearly complete obstruction (>95% RAS). Baseline HIP studies, however, demonstrated in this group classic findings, compatible with the diagnosis of RVH, although captopril did not modify them further (Fig. 4).

3. HIP recognized all 14 RVH kidneys with severe (60–95%) RAS by showing a captopril induced increase in the 20 min cortical residual activity (Figs. 1 and 2), whereas DTPA demonstrated a captopril suppressing effect of glomerular filtration in only ten (Fig. 2) of them. With DTPA, no appreciable change from the baseline study was evident in four kidneys of patients with renal insufficiency, although HIP demonstrated a captopril effect in these patients. Moreover, in another three kidneys, included in the ten above, the differences between the pre- and the postcaptopril DTPA graphs were only slight and without appreciable changes in imaging (Fig. 1).

4. Captopril had no effect on HIP or DTPA studies in patients with mild, insignificant (<60%) RAS, and a normal blood pressure or normal renal vein renin activities (Fig. 3).

5. HIP and DTPA studies showed no effect of captopril on kidneys with normal arteries, including hypoplastic kidneys, and on the normally perfused portion of kidneys with a branch stenosis of the RA (Fig. 2).

6. In patients with a decreased renal function baseline HOP and DTPA studies were abnormal. Although captopril may have little effect in these kidneys, HIP unlike DTPA could differentiate the contribution of RAS vs intrinsic renal disease in the decrease in function (Fig. 4). Thus, when the results of HIP and DTPA were compared using renographic patterns observed with and without captopril, HIP was a more specific indicator of RVH than DTPA ($p < 0.001$).

Clearance studies without imaging (*26*) and measurements of peripheral vein renin levels (*27*) before and after captopril have been proposed for the diagnosis of RVH. In this series of patients, clearance studies (ERPF) were useful in distinguishing only some patients with RVH (Figs. 1 and 2) but not those with a unilateral abnormal baseline study and no effect of captopril (Fig. 4). Bilateral RVH or RVH in renal homografts was associated with a decrease in total ERPF after captopril; whereas patients without RVH showed no decrease in ERPF after captopril, so did some patients with unilateral RVH. Inconsistent changes in ERPF and GFR after captopril have been reported (*28*). Measurement of peripheral blood renin levels is not useful in indicating the existence of RVH (*29*). When used after captopril, the test was found to be insensitive in patients with compromized renal function (*27*). In contrast, captopril HIP renography was successful in this category of patients both as a screening and a lateralizing test.

Our experience generally agrees with previous reports on captopril scintigraphy (*13,17*). Captopril HIP camera renography may be specific for RVH in predicting the potential benefit of renal angioplasty (*13*). Based on the pathophysiologic considerations outlined above, it is reasonable to expect that when captopril decreases the function of the kidney, renal angioplasty would be effective in curing the hypertension. This was the case, in five patients in our series.

Our approach brings into focus the possibility of completing the two phases of the test in a single day with one dose of captopril. The results also suggest that only the postcaptopril study may be necessary for screening purposes. Considering pre- and postcaptopril HIP studies, all RVH-related kidneys either did not visualize or had post captopril HIP cortical retention of activity at 20 min in excess of 30% of their peak cortical activity. Using these two parameters in a postcaptopril HIP test, 15 of 18 patients without RVH and 18 out of 18 with RVH would have been diagnosed correctly. Thus, baseline studies would have been needed to differentiate three of the 18 patients without RVH from the patients with RVH. DTPA studies in this series of patients cannot be approached in a similar manner, unless the patients with decreased renal function are first excluded.

There were no side effects associated with captopril in this series. Blood pressure decreased transiently after captopril in most patients without RVH and in all patients with RVH. It is, however, recommended that an intravenous infusion of saline or a heparin lock be in place in captopril studies. Blood pressure should be monitored particularly closely in patients receiving diuretics or with a high probability of renin-dependent hypertension (*30*).

Our observations emphasize the value of HIP scintigraphy in patients with renal insufficiency. Measuring the cortical transit or retention of HIP with captopril

provides a uniquely sensitive indicator which is not shared by other radiopharmaceuticals including DTPA (*20*). Further experience is needed to assess the sensitivity of the test, particularly in patients with bilateral arterial disease and compromised renal function, in children, and in patients with dysplasias, pyelonephritis, obstructive uropathy, renal vein thrombosis and other abnormalities associated with an abnormal baseline renogram.

ACKNOWLEDGMENTS

The authors thank Mrs. Gilda Manicourt for typing the manuscript, Mr. Christopher Fletcher and Mr. Steve Arnyek for the composition and printing of the images, and Ms. Efrosyni Sfakianaki for the art work.

REFERENCES

1. Vaughan ED, Case DB, Pickering TG, et al. Clinical evaluation of renovascular hypertension and therapeutic decisions. *Urol Clin North Am*, 1984; 3:393–397.
2. Eyler WR, Clark MD, Garman JE. Angiography of the renal areas including a comparative study of renal arterial stenosis in patients with and without hypertension. *Radiology* 1962; 78:879–891.
3. Holley KE, Hunt JC, Brown AL, et al. Renal artery stenosis: a clinical-pathologic study in normotensive patients. *Am J Med*, 1964; 37:14–22.
4. Foster JH, Maxwell MH, Franklin SS, et al. Renovascular occlusive disease: results of operative treatment. *JAMA* 1975; 231:1043–1048.
5. Thornburg JR, Stanley JC, Fryback DG. The nonusefulness of hypertensive urography: renal arteriography as an alternative strategy [Abstract]. *Am J Roentgenol* 1979; 132:1029.
6. Arlat I, Rosenthal J, Adam WE, et al. Predictive value of radionuclide methods in the diagnosis of unilateral renovascular hypertension. *Cardiovasc Radiol* 1979; 2:115–125.
7. Sfakianakis GN, Zilleruelo G, Thompson T, et al. 99m-Tc glucoheptonate scintigraphy in a case of renal vein thrombosis. *Clin Nucl Med* 1985; 10:75–79.
8. Pickering TG, Sos TA, Vaughan ED Jr., et al. Predictive value and changes of renin secretion in hypertensive patients with unilateral renovascular disease undergoing successful renal angioplasty. *Am J Med* 1984; 76:398–404.
9. Vaughan ED Jr, Case DB, Pickering TG, et al. Clinical evaluation of renovascular hypertension and therapeutic decisions. In: Symposium on renal vascular disease. *Urol Clin North America* 1984; 11:393–407.
10. Case DB, Laragh JH. Reactive hyperreninemia following angiotensin blockade with either saralasin or converting enzyme inhibitor: a new approach to screen for renovascular hypertension. *Ann Intern Med* 1979; 91:153–1160.
11. Lyons DF, Streck WF, Kem DC, et al. Captopril stimulation of differential renins in renovascular hypertension. *Hypertension* 1983; 5:615–622.
12. Re R, Noveline R, Escourrou MT, et al. Inhibition of angiotensin-converting enzyme for diagnosis of renal-artery stenosis. *N Engl J Med* 1978; 298:582–586.
13. Wenting GJ, Tan-Tjiong HL, Derkx FHM, et al. Split renal function after captopril in unilateral renal artery stenosis. *Br Med J* 1984; 288:886–890.
14. Majd M, Potter BM, Guzzetta PC, et al. Effect of captopril on efficacy of renal scintigraphy in detection of renal artery stenosis [Abstract]. *J Nucl Med* 1983; 24:P23.
15. Filipeski S, Bar-Hndziak E, Malanowska S. Diagnosis of renovascular hypertension. *Pol Arch Med Wewn* 1979; 62:455–459.
16. Kremer-Hovinga TK, Beukhof JR, Van Luyk WHJ, et al. Reversible diminished renal 99m-Tc-DMSA uptake during converting-enzyme inhibition in a patient with renal artery stenosis. *Eur J Nucl Med* 1984; 9:144–146.
17. Geyskes GG, Oei HY, Faber JAJ. Renography: prediction of blood pressure after dilatation of renal artery stenosis. *Nephron* 1986; 44(suppl 1):54–59.
18. Dubovsky EV, Russell CD. Quantitation of renal function with glomerular and tubular agents. *Semin Nucl Med* 1982; 12:308–329.
19. Gates GF. Glomerular filtration rate: estimation from fractional renal accumulation of 99m Tc-DTPA (stannous). *Am J Roentgenol* 1982; 138:565–570.
20. Vaughan ED, Buhler FR, Laragh JH, et al. Renovascular hypertension: renin measurements to indicate hypersecretion and contralateral suppression, estimate of renal plasma flow, and score for surgical curability. *Am J Med* 1973; 55:402–414.
21. Duncan RC, Knapp R, Miller NC. Introductory biostatistics for the health sciences, 2nd ed. New York: John Wiley and Sons, Inc., 1983.
22. Nally JV, Clarke HS, Windham JP, et al. Technetium-99m DTPA renal flow studies in Goldblatt hypertension. *J Nucl Med* 1985; 26:917–924.
23. Hall JE, Guyton AC, Jackson TE, et al. Control of glomerular filtration rate by renin-angiotensin system. *Am J Physiol* 1977; 233:F366–372.
24. Anderson WP, Korner PI, Johnston CI. Acute angiotensin II-mediated restoration of distal renal artery pressure in renal artery stenosis and its relationship to the development of sustained one-kidney hypertension in conscious dogs. *Hypertension* 1979; 1:292–298.
25. Nally JV, Clarke HS, Grecos GP, et al. Effect of captopril on Tc-99m-diethyletriaminepentaacetic acid renograms in two-kidney, one clip hypertension. *Hypertension* 1986; 8:685–693.
26. Dubovsky EV, Curtis JJ, Luke RG, et al. Effect of captopril on ERPF in differential diagnosis of hypertension in renal transplant recipients [Abstract]. 1985; *J Nucl Med* 26:P73.
27. Muller FB, Sealey JE, Case DB, et al. The captopril test for identifying renovascular disease in hypertensive patients. *Am J Med* 1986; 80:633–644.
28. Miyanori I, Yoshuara S, Takeda Y, et al. Effects of converting enzyme inhibition on split renal function in renovascular hypertension. *Hypertension* 1986; 8:415–421.
29. Bourgoignie JJ, Kurz S, Catanzaro FJ, et al. Renal venous renin in hypertension. *Am J Med* 1970; 48:332–342.
30. Hodsman GP, Isles CG, Murray GD, et al. Factors related to first dose hypotensive effect of captopril prediction and treatment. *Br Med J* 1983; 286:832–834.