Renal Artery Stenosis Detection by Combined Gates' Technique and Captopril Test in Hypertensive Patients

Alberto Cuocolo, Salvatore Esposito, Massimo Volpe, Luigi Celentano, Arturo Brunetti, and Marco Salvatore

Istituto di Scienze Radiologiche, Cattedra di Medicina Nucleare, and I Clinica Medica, II Facolta' di Medicina, Universita' di Napoli, Italy

We studied 11 hypertensive patients by a radionuclide technique using Gates' method with [^{99m}Tc]DTPA to investigate the acute effects of captopril on glomerular filtration rate (GFR). Five patients had hypertension with unilateral renal artery stenosis (RAS) angiographically documented and six patients had essential hypertension (EH). Total and split GFR were determined under control conditions and after oral administration of captopril (50 mg). In the patients with RAS, captopril induced a significant decrease of GFR in the stenotic kidneys (from 42.4 ± 4 to 29.6 ± 3 ml/min, $p < 0.01$), while no changes were observed in the nonstenotic kidneys (from 61.2 ± 3 to 61.6 ± 5 ml/min, NS). Total GFR was 103.6 ± 5 ml/min under control conditions and decreased to 91.8 ± 6 ml/min after captopril ($p < 0.05$). No significant changes of GFR were detected after captopril administration in patients with EH. In a separate group of ten patients with EH, good correlation between 24-hr creatinine clearance and fractional uptake of [^{99m}Tc]DTPA was obtained. Good reproducibility of this radionuclide technique was also shown. This study demonstrates that the computed radionuclide GFR determination coupled with the captopril test allows one to unmask angiotensin II-dependent renal function and hemodynamic changes. This technique can be useful in clinical practice for identifying patients with renovascular hypertension.

J Nucl Med 30:51–56, 1989

Detection of correctable renal artery stenosis (RAS) in hypertensive patients has received renewed interest given the recent advances in surgical and percutaneous angioplasty techniques (*1,2*). Numerous tests have been suggested to detect renovascular hypertension, but many have a limited sensitivity or specificity (*3–10*).

Reversible renal failure or a deterioration in renal function associated with angiotensin-converting enzyme (ACE) inhibition, induced by captopril treatment, is known to occur in patients with bilateral RAS or arterial stenosis in a solitary or transplanted kidney (*11, 12*). Recent studies have shown that captopril also may decrease the glomerular filtration rate (GFR) of the kidney affected by RAS in the presence of an intact contralateral kidney. This effect is usually not apparent clinically because of the compensatory function of the other kidney, but can be revealed by radionuclide methods (*13–15*). Gates (*16,17*) described a simple technique based upon determining the empiric correlation between the renogram and GFR as measured by creatinine clearance. Once such a relationship is established, it can be used prospectively to estimate GFR from the renogram. The basic renogram parameter used by Gates was the sum of the counts during a specific time period, i.e., the area under the renogram curve. This method allows determination of GFR for each kidney and derives values for global renal function without blood or urine sampling (*16–18*).

The aim of the present study was to evaluate the effects of ACE inhibition on the renal function of individual kidneys, assessed by this rapid and noninvasive radionuclide technique, in patients with essential hypertension (EH) and in patients with hypertension with angiographically documented RAS.

Received Apr. 11, 1988; revision accepted July 22, 1988.

For reprints contact: Alberto Cuocolo, MD, Dept. of Nuclear Medicine, National Institutes of Health, Building 10-Room 1C401, 9000 Rockville Pike, Bethesda, MD 20892.

MATERIALS AND METHODS

Subjects

This study was carried out in 11 hypertensive patients divided into two groups: Group 1 included five patients with hypertension with unilateral RAS (three female and two male, mean age 43 ± 6 yr); Group 2 included six patients with EH (two female and four male, mean age 42 ± 3 yr). Renal arteriography was performed prior to the radionuclide study in all patients. Unilateral RAS (60–90% narrowing of the main branch) was demonstrated on arteriograms in the five patients of Group 1. Patients with very severe RAS (>90%) were not included in the study. In the six patients of group 2, arteriography showed normal renal arteries.

All patients were fully informed about the procedure and the aims of the study, and consent was obtained from each of them.

Blood pressure (BP) was measured three times, at least 1 wk apart, with the patients in the supine position after 5 min of rest in a darkened room, with a mercury sphygmomanometer as recommended by the American Heart Association (*19*). All patients presented BP values >160/90 mmHg and were hospitalized for at least 4 wk while the diagnosis of RAS or EH was made. Other secondary forms of hypertension were ruled out on the basis of history, physical examination, and routine screening tests. None of the patients had taken any medication for at least 2 wk preceding the study, and none received medication during the period of the study. In the 2 wk preceding the study, as well as during the study, each patient consumed a daily isocaloric diet (30 cal/kg), containing 160 mEq sodium and 70 mEq potassium. All patients had normal serum creatinine levels at the time of scintigraphic evaluation. Fundoscopic examination, electrocardiography, chest roentgenography, and echocardiography were used to diagnose each patient's hypertension as either stage I or II according to the World Health Organization Classification.

Renal Scintigraphy

The computed radionuclide GFR of individual kidneys was assessed 2–3 min after a single i.v. injection of 3 mCi (111 MBq) of technetium-99m diethylene-triaminepentaacetic acid ([^{99m}Tc]DTPA) using the method described by Gates (*16,17*). The injected dose was measured by counting the syringe with a gamma camera (GE, Starport) using standardized geometry (at 30 cm). Renal scintigraphy was performed with the same gamma camera equipped with a low-energy, parallel hole collimator. The patients were positioned upright before the gamma camera. Data acquisition was initiated at the moment of injection and recorded in computer memory every 15 sec for 6 min. At the end of the study, each kidney was outlined by a region of interest. To calculate GFR, the fractional uptake was first determined by the computer then related to the clearance values (*16,17*): fractional uptake ([^{99m}Tc]DTPA) 2–3 min:

$$\frac{\text{kidney counts} - \text{background}}{e^{-\mu y}} \times 100,$$
$$\text{counts of injected dose}$$

where y is the renal depth calculating according to Tonnesen et al. (*20*): left kidney depth = 13.2 (height/weight) + 0.7, right kidney depth = 13.3 (height/weight) + 0.7, and μ is the attenuation coefficient for ^{99m}Tc in tissue equivalent (μ = 0.153). Fractional uptake was related to clearance value by the following empiric regression equation (*17*):

GFR = fractional uptake ([^{99m}Tc]DTPA) × 9.81270 − 6.82519.

Study Protocol

All patients of Group 1 (RAS) and Group 2 (EH) had a baseline and a postcaptopril computed radionuclide GFR study. The two studies were performed 24 hr apart, and the second was started 1 hr after a single dose of 50 mg captopril. All patients were seated for at least 30 min before captopril was administered. To facilitate absorption, the captopril tablet was crushed and dissolved in 10 ml of water immediately prior to administration. BP and heart rate (HR) were monitored every 10 min and again 1 hr after study completion.

In order to assess the accuracy of the technique, we performed an ancillary study in ten patients with EH (Group 3: eight female and two male, mean age 48 + 4 yr). These patients were asked to follow the same guidelines pertaining to diet and drug intake as those in the other two groups. In all patients, the GFR was determined by both the radionuclide method and a conventional 24-hr creatinine clearance, as previously described (*21*). Finally, the reproducibility of the radionuclide computed GFR was determined by performing paired renograms in the same ten patients with EH 24 hr apart. These patients had stable renal function as judged by creatinine clearance.

Statistical Analysis

Statistical comparisons were by Student's t-test, either paired or unpaired; a p value < 0.05 was required for significance. Data are expressed as mean ± s.e.m. Linear regression analysis was performed to determine the correlation between the computed GFR data and the 24-hr creatinine clearance, and between data obtained from the paired computed GFR studies performed under control conditions in the patients of Group 3.

RESULTS

In Table 1 are shown the baseline hemodynamic and humoral measurements recorded in the study population.

Captopril Test

Systolic and diastolic BP were significantly reduced after captopril in both Groups 1 and 2, while HR did not change (Table 2). In patients with hypertension with unilateral RAS (Group 1), GFR for the stenotic kidneys was 42.4 ± 4 ml/min and was significantly less than that of the nonstenotic kidneys 61.2 ± 3 ml/min ($p < 0.01$). Although the latter value did not change significantly after captopril administration (61.6 ± 5 ml/min, NS compared with the pretreatment level), the GFR of the RAS group decreased further to 29.6 ± 3 ml/min ($p < 0.01$, compared with pretreatment level)

TABLE 1
Hemodynamic and Humoral Measurements Recorded in Control Conditions in the Three Groups of Patients Studied

	Group 1 (n = 5)	Group 2 (n = 6)	Group 3 (n = 10)
Systolic BP (mmHg)	168 ± 5	163 ± 3	170 ± 6
Diastolic BP (mmHg)	107 ± 5	98 ± 3	102 ± 3
Heart Rate (bpm)	74 ± 3	77 ± 4	76 ± 3
GFR (ml/min)	103.6 ± 5	100.8 ± 6	97.5 ± 8
BUN (mg/dl)	15 ± 3	16 ± 2	16 ± 3
Creatinine (mg/dl)	1.1 ± 0.1	1.02 ± 0.02	1.1 ± 0.06
Serum Na^+ (mEq/l)	141 ± 2	142 ± 2	142 ± 2
Serum K^+ (mEq/l)	4.1 ± 0.2	4.3 ± 0.2	4.1 ± 0.2
PRA (ng/ml/hr)	4.8 ± 1.9	1.3 ± 1.1	1.2 ± 0.9
ALDO (ng/dl)	6.9 ± 2.6	7.3 ± 4.2	7.4 ± 4.2

BP = Blood pressure; GFR = Glomerular filtration rate; BUN = Blood urea nitrogen; PRA = Plasma renin activity; ALDO = Plasma aldosterone concentration.

(Fig. 1). Total GFR in control conditions was 103.6 ± 5 ml/min and decreased to 91.8 ± 6 ml/min after captopril ($p < 0.05$) (Table 2 and Fig. 1). The data for split renal function for individual patients of Group 1 before and after captopril are shown in Figure 2.

Figure 3 shows the effects of captopril on the total and split GFR for the patients with EH (Group 2). These parameters did not change significantly after captopril administration. In particular, the GFR of the left kidneys was 49.5 ± 5 ml/min in control conditions and 52.0 ± 5 ml/min after treatment; the baseline GFR for the right kidneys was 51.1 ± 4 ml/min and during ACE inhibition was 54.8 ± 4 ml/min. Total GFR was 100.8 ± 6 ml/min in control conditions and 106.8 ± 5 ml/min after captopril administration (Table 2 and Fig. 3).

Ancillary Study

A good correlation was observed between creatinine clearance and GFR calculated by Gates' formula in ten patients with EH (Group 3) ($r = 0.913$, $p < 0.001$, $y = 11.2 \pm 0.879 \times$, s.e.e. = 10.4) for global renal function (Fig. 4). The mean creatinine clearance was 97.2 ± 8 ml/min, the mean radionuclide GFR was 96.7 ± 8 ml/min. No statistically significant difference was observed between creatinine clearance and radionuclide GFR determination. Finally, the reproducibility of computed GFR, determined by performing paired renograms in the same group of ten patients with EH (Group 3), was excellent ($r = 0.930$, $p < 0.001$, $y = 24.1 + 0.779$, s.e.e. = 8.5) (Fig. 5). The mean GFR 1 was 97.5 ± 8 ml/min, the mean GFR 2 was 99.7 ± 7 ml/min. No significant difference was observed between GFR 1 and GFR 2.

DISCUSSION

Although several authors (*13–15,22–25*) have reported the application of noninvasive radionuclide studies of the kidney with ACE inhibition in hypertensive patients with RAS, the acute effects of captopril administration on GFR assessed by Gates' technique have never been studied in humans. However, this technique for the determination of global and split renal GFR has been successfully used by Kopecky et al. (*26*) and McAfee et al. (*27*) in models of experimental hypertension. Gates and other authors validated this technique with creatinine and inulin clearance meas-

TABLE 2
Effects of Captopril on Systolic and Diastolic Blood Pressure, Heart Rate, and Glomerular Filtration Rate in Patients with Hypertension with Unilateral RAS (Group 1) and in Patients with EH (Group 2)

	SBP		DBP		HR		GFR	
	Control	Captopril	Control	Captopril	Control	Captopril	Control	Captopril
Group 1 (n = 5)	168 ± 5	149 ± 5†	107 ± 5	88 ± 4†	74 ± 3	75 ± 4	103.6 ± 5	91.8 ± 6*
Group 2 (n = 6)	163 ± 3	150 ± 3†	98 ± 3	89 ± 3*	77 ± 4	76 ± 4	100.8 ± 6	106.8 ± 5

RAS = Renal artery stenosis; EH = Essential hypertension; SBP = Systolic blood pressure (mmHg); DBP = Diastolic blood pressure (mmHg); HR = Heart rate (bpm); GFR = Glomerular filtration rate (ml/min). * Indicates $p < 0.05$ and † indicates $p < 0.01$, compared with the pretreatment values.

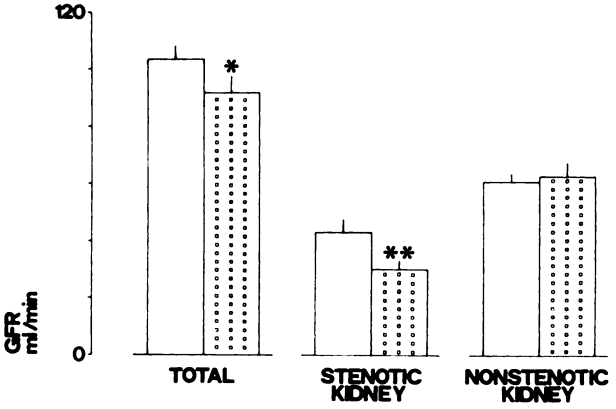

FIGURE 1
Effects of captopril on total and split GFR in five patients with hypertension with unilateral RAS. Each bar represents mean ± se. * and ** Indicate $p < 0.05$ and $p < 0.01$ compared with the pretreatment values. (□) control; (▨) captopril.

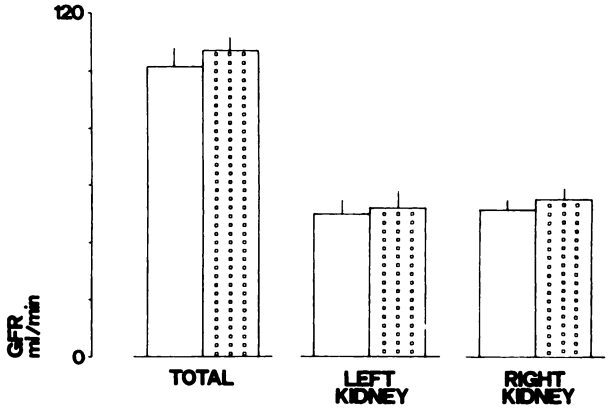

FIGURE 3
Effects of captopril on total and split GFR in six patients with EH. Each bar represents mean ± s.e. (□) control; (▨) captopril.

urements for global (*16,17*) and split (*18*) renal function. A positive correlation between global GFR measured by radionuclide methods and fractional uptake of [^{99m}Tc]DTPA by the kidneys already has been demonstrated by previous studies (*27,28*). The results obtained in our ancillary study, performed in ten patients with EH and preserved renal function (Group 3), show a significant relationship between the 24-hr creatinine clearance and computed radionuclide GFR determination. The reproducibility of the method is excellent as shown by comparing the results of repeated studies on the same group of patients performed 24 hr apart under control conditions. The good accuracy and reproducibility of the computed radionuclide GFR determination render this technique of renal function measurement extremely useful in clinical practice.

Several factors can interfere with the fractional uptake determination and calculation of GFR. Recently, Ginjaume et al. (*29*) found no correlation between global GFR measured by the one injection-two blood samples technique of Brochner-Mortensen (*30*) and [^{99m}Tc]DTPA fractional uptake, concluding that the Gates' method for GFR determination was unreliable. For these authors, kidney depth, calculated by Tonnesen's formula (*20*), is the major source of error. By contrast, Chachati et al. (*18*) demonstrated a good correlation between inulin clearance and the fractional uptake of [^{99m}Tc]DTPA, whether kidney depth was calculated by Tonnesen's formula or measured by scintigraphic lateral views. Tonnesen's method of estimating renal depth from a patient's height and weight has been used successfully by Schlegel et al. (*31,32*) for many years determining effective renal plasma flow and GFR, and, as used in the study that Gates originally reported (*16*), was shown to improve the accuracy.

The intravascular and extracellular fluid volume and cardiac output are other factors which affect the 2-

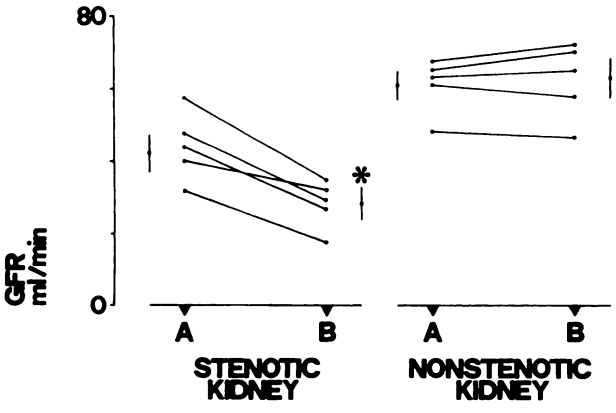

FIGURE 2
Individual data of split GFR in the stenotic and nonstenotic kidneys of five patients with hypertension with unilateral RAS before (A) and after captopril (B). * Indicates $p < 0.01$ compared with the pretreatment values.

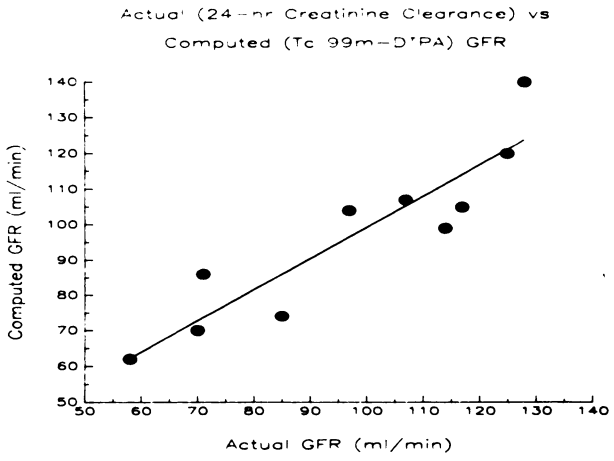

FIGURE 4
Relationship between 24-hr creatinine clearance and [^{99m}Tc]DTPA GFR in ten patients with EH ($r = 0.913$, $p < 0.001$).

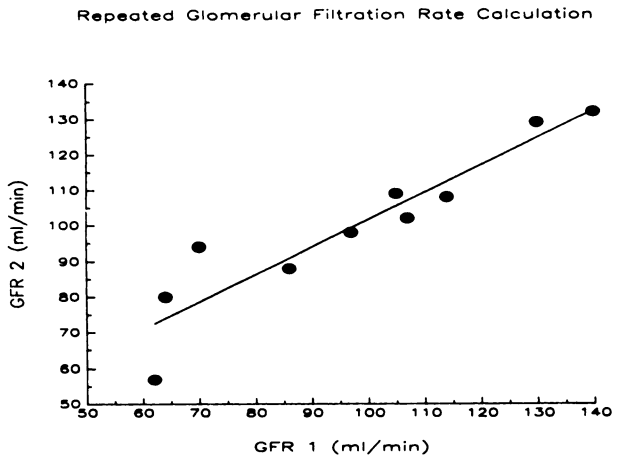

FIGURE 5
The reproducibility of radionuclide computed GFR was determined by performing paired renograms in ten patients with EH 24 hr apart in control conditions. GFR 1 = First measurement; GFR 2 = Second measurement ($r = 0.930$, $p < 0.001$).

3 min kidney accumulation of the injected radionuclide and its clearance. The hypertensive patients we studied had no clinical evidence of any increase in the intravascular or extracellular fluid volume and were not in heart failure. In addition, as recently suggested by Gates (*33*), too large a dose of radionuclide, which results in an inaccurate preinjection syringe count determination or an inaccurate transmission of syringe count information from camera to computer, also represents potential sources of error. These factors played little role in our study, but should be kept in mind when the situation arises.

We used 50 mg captopril because previous studies (*34,35*) demonstrated that some patients with proved renovascular disease failed to exhibit any blood pressure response with the 25 mg captopril test. This may be explained by the fact that with the lower dose an incomplete blockade of renin-angiotensin system may be overcome by the vigorous renin response that is characteristic of renovascular disease. In contrast, the 50 mg dose is constantly sufficient to induce a sustained blockade of ACE (*34*).

Our experience in using the Gates' method coupled with the captopril test in hypertensive patients indicates that it is safe and without unpleasant side effects and, therefore, is applicable for outpatient evaluation. This radionuclide technique as described herein may represent a useful approach for identifying patients with renovascular disease from a general population of patients with uncomplicated hypertension.

Our results observed in patients of Group 1 demonstrate that a single oral dose of captopril reduces GFR in the stenotic kidneys of patients with hypertension and unilateral RAS. However, in the contralateral unaffected kidney GFR was unaltered. As a consequence, there was a slight but statistically significant decrease in global GFR following ACE inhibition by captopril. The hemodynamic changes in the nonstenotic kidneys were similar to those seen in the group of patients with EH.

The decrease of GFR obtained after captopril administration seems to be related to ACE inhibition-induced deterioration of GFR of the stenotic kidney (*15,22,23*). These findings are consistent with the hypothesis that GFR and intrarenal resistance of the stenotic kidney are mediated by angiotensin II-dependent efferent arteriolar constriction, and suggest that ACE inhibition may accentuate angiotensin II-dependent renal hemodynamic and functional changes of RAS. The observation made in this study confirms previous reports in both experimental and human models by several investigators (*15,22–27*) that ACE inhibition with captopril is capable of altering renal function assessed by radionuclide studies thus improving the diagnostic accuracy of these studies in the evaluation of patients with suspected renovascular hypertension. However, an estimation of the sensitivity of captopril renography is affected by several problems related to the diagnostic recognition of this disease (*36*). Further experience is needed to assess the sensitivity of the technique, particularly in patients with different degrees of RAS, with bilateral arterial disease, and with impaired renal function.

In conclusion, on the basis of our results, we suggest that the determination of the fractional uptake of [^{99m}Tc]DTPA between 2–3 min performed in control conditions and 1 hr after oral captopril administration allows one to unmask angiotensin II-dependent renal function and hemodynamic changes. This test offers promise in identifying patients with hypertension secondary to RAS. This method can be useful in clinical practice, and may be suitable for the screening of patients with renovascular hypertension. Increasing the number of patients tested in a prospective study using the same criteria would help to define the sensitivity and the specificity more precisely.

ACKNOWLEDGMENTS

The authors thank Dr. Ronald D. Neumann, Chief of the Department of Nuclear Medicine, National Institutes of Health, for his valuable comments.

REFERENCES

1. Dzau V, Gibbons G, Levin D. Renovascular hypertension: an update on pathophysiology, diagnosis and treatment. *Am J Nephrol* 1983; 3:172–184.
2. Novick A, Straffon R, Stewart B, Gifford R, Vidt D. Diminished operative morbidity and mortality in renal revascularization. *JAMA* 1981; 246:749–753.
3. Vaughan ED, Case DB, Pickering TG, et al. Clinical evaluation of renovascular hypertension and therapeutic decisions. *Urol Clin North Am* 1984; 3:339–397.

4. 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.
5. 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.
6. Foster JH, Maxwell MH, Franklin SS, et al. Renovascular occlusive disease: results of operative treatment. *JAMA* 1975; 231:1043–1048.
7. Thornburg HR, Stanley JC, Fryback DG. The non-usefulness of hypertensive urography: renal arteriography as an alternative strategy [Abstract]. *Am J Roentgenol* 1979; 132:1029.
8. 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.
9. Sfakianakis GN, Zilleruelo G, Thompson T, et al. Tc-99m glucoheptonate scintigraphy in a case of renal vein thrombosis. *Clin Nucl Med* 1985; 10:75–79.
10. 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.
11. Hricik DE, Browning DJ, Kopelman R, Goorno W, Madias N, Dzau V. Captopril-induced functional renal insufficiency in patients with bilateral renal artery stenosis or renal artery stenosis in a solitary kidney. *N Engl J Med* 1983; 308:373–376.
12. Curtis JJ, Luke RG, Whelchel JD, et al. Inhibition of angiotensin-converting enzyme in renal transplanted recipients with hypertension. *N Engl J Med* 1983; 308:377–381.
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. Geyskes GG, Oei HY, Puylaert CBAJ, Dorhout Mees EJ. Renovascular hypertension identified by captopril-induced changes in the renogram. *Hypertension* 1987; 9:451–458.
15. Nally JV, Clarke HS, Grecos GP, et al. Effects of captopril on Tc-99m DTPA renograms in two-kidney, one clip hypertension. *Hypertension* 1986; 8:685–693.
16. Gates GF. Glomerular filtration rate: estimation from fractional renal accumulation of Tc-99m DTPA (stannous). *Am J Roentgenol* 1982; 138:565–570.
17. Gates GF. Split renal function testing using Tc-99m DTPA. A rapid technique for determining differential glomerular filtration. *Clin Nucl Med* 1983; 8:400–407.
18. Chachati A, Meyers A, Godon JP, Rigo P. Rapid method for the measurement of differential renal function: validation. *J Nucl Med* 1987; 28:829–836.
19. Kirkendall WM, Burton MC, Epstein FM, Freis ED. Recommendations for human blood pressure determination by sphygmomanometers. *Circulation* 1967; 36:980–986.
20. Tonnesen KH, Munck O, Hald T, Mogensen P, Wolf H. Influence on the renogram of variation on skin to kidney distance and the clinical importance thereof. In: Zum Winkel K, Blaufox MD, Bretano JLF, eds. *Radionuclides in nephrology.* Stuttgart: George Thieme; 1975:79–86.
21. Trimarco B, De Simone A, Cuocolo A, et al. Role of prostaglandins in the renal handling of a salt load in essential hypertension. *Am J Cardiol* 1985; 55:116–121.
22. Dubovsky EV, Curtis JJ, Luke RG, et al. Captopril test as predictor of curable hypertension in renal transplant recipients [Abstract]. *J Nucl Med* 1986; 27:576.
23. Nally JV, Clarke HS, Gupta BK, et al. Captopril renography in two kidney and one kidney Goldblatt hypertension in dogs. *J Nucl Med* 1987; 28:1171–1179.
24. Sfakianakis GN, Bourgoignie JJ, Jaffe D, Kyriakides G, Perez-Stable E, Duncan RC. Single-dose captopril scintigraphy in the diagnosis of renovascular hypertension. *J Nucl Med* 1987; 28:1383–1392.
25. Fommei E, Ghione S, Palla L, et al. Renal scintigraphic captopril test in the diagnosis of renovascular hypertension. *Hypertension* 1987; 10:212–220.
26. Kopecky RT, Thomas FD, McAfee JG. Furosemide augments the effects of captopril on nuclear studies in renovascular stenosis. *Hypertension* 1987; 10:181–188.
27. McAfee JG, Kopecky RT, Thomas FD, Hellwig B, Roskopf M. Comparison of different radioactive agents for the detection of renovascular hypertension with captopril in a rat model. *J Nucl Med* 1988; 29:509–515.
28. Thomas FD, McAfee JG, Lyons B, Gagne GM, Ritter C. Computer-quantitated renal uptake vs. plasma clearance of Tc-99m DTPA in rats with and without glomerular damage [Abstract]. *J Nucl Med* 1983; 24:80.
29. Ginjaume M, Casey M, Barker F, Duffy G. Measurement of glomerular filtration rate using technetium-99m DTPA. *J Nucl Med* 1985; 26:1347–1348.
30. Brochner-Mortensen J. Routine methods and their reliability for assessment of glomerular filtration rate. *Dan Med Bull* 1978; 25:181–202.
31. Schlegel JU, Hamway SA. Individual renal plasma flow determination in 2 minutes. *J Urol* 1976; 116:282–285.
32. Schlegel JU, Halikiopoulos HL, Prima R. Determination of filtration fraction using the gamma scintillation camera. *J Urol* 1979; 122:447–450.
33. Gates GF. Measurement of glomerular filtration rate using technetium-99m DTPA. *J Nucl Med* 1985; 26:1348–1349.
34. 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.
35. Case DB, Atlas SA, Laragh JH. Reactive hyper-reninaemie to angiotensin blockade identifies renovascular hypertension. *Clin Sci* 1979; 57:3135–3165.
36. Maxwell MH, Waks AU. Evaluation of patients with renovascular hypertension. *Hypertension* 1984; 6:589–592.