Aspirin Renography and Captopril Renography in the Diagnosis of Renal Artery Stenosis

Peter J.G. van de Ven, John M.H. de Klerk, Ilse J.R. Mertens, Hein A. Koomans, and Jaap J. Beutler

Department of Nephrology and Hypertension and Department of Nuclear Medicine, University Medical Center Utrecht, Utrecht, The Netherlands

Preliminary data suggest that aspirin renography is more sensitive than captopril renography for indicating renal artery stenosis (RAS). Considering that aspirin, compared with captopril, reduces renal blood flow and, thus, tubular tracer delivery in poststenotic kidneys, aspirin renography is expected to be more useful, particularly if tubular tracers are used. **Methods:** We prospectively compared aspirin renography (20 mg/kg orally) and captopril renography (25 mg orally) with ^{99m}Tc-mercaptoacetyltriglycine in 75 consecutive patients suspected of having RAS. **Results:** RAS, diagnosed as stenosis of more than 50% on angiography, was found unilaterally in 34 patients and bilaterally in 17 patients. RAS was absent in 24 patients. The sensitivities for unilateral RAS or bilateral RAS (i.e., stenosis that was at least unilateral) were, respectively, 88% and 88% for captopril renography and 82% and 94% for aspirin renography (not significant). The overall specificity was 75% for captopril renography and 83% for aspirin renography (not significant). Tracer uptake ratios, time to peak activity, and percentage of 20-min tracer retention were also not significantly different for captopril and aspirin renography. Subgroup analysis of modest (50–75%) and severe (≥75%) RAS, or of plasma creatinine greater than 120 μmol/L, also showed no difference between captopril and aspirin renography. **Conclusion:** We conclude that for identification of RAS, the usefulness of aspirin renography equals, but does not surpass, that of captopril renography.

Key Words: renal artery stenosis; renography; aspirin; captopril; hypertension

J Nucl Med 2000; 41:1337–1342

Renal artery stenosis (RAS) is the most common cause of secondary hypertension. Its prevalence varies from 5% in the nonselected hypertensive population (*1*) to approximately 30% in elderly patients with drug-refractory hypertension (*2,3*). In this category, RAS, usually caused by atherosclerosis, is recognized increasingly as a cause of end-stage renal failure (*4–6*). Angioplasty or stenting of the stenotic lesion reduces the need for antihypertensive medication (*7,8*) and may attenuate the progression of renal insufficiency (*9*).

Intra-arterial angiography is the gold standard for the diagnosis. However, this technique is invasive, harbors the risk of complications, and is costly (*10*). Therefore, noninvasive tests have been developed, of which captopril-enhanced renography is the most widely used. A review of 9 studies (*11*) indicated that the sensitivity of captopril renography to detect RAS averaged 84% (range, 71%–94%). This finding implies that a substantial number of cases are being overlooked.

Preliminary data indicate that aspirin-enhanced renography with hippurate may be more sensitive for detecting unilateral RAS (*12*). Perhaps aspirin, which reduces both renal blood flow and glomerular filtration, more effectively impairs the excretion of a tracer whose excretion depends on both filtration and tubular secretion. However, the comparison concerned only 5 patients, and the sensitivity of captopril renography was unusually low (40%) (*12*). Besides, patients with bilateral RAS were not included, and the reliability of captopril renography to detect bilateral RAS is relatively low (*13–16*). To know whether aspirin renography performs better would be useful.

We therefore compared captopril renography with aspirin renography in 75 consecutive patients scheduled for arteriography because of suspected RAS. By this approach, we obtained data from patients with unilateral or bilateral RAS and patients without RAS. We used ^{99m}Tc-mercaptoacetyltriglycine (MAG3), which, like hippurate, depends for its excretion mainly on tubular secretion.

MATERIALS AND METHODS

Patients

Seventy-five consecutive patients with known (n = 28) or suspected (n = 47) RAS and scheduled for diagnostic and therapeutic arteriography underwent, successively, captopril renography and aspirin renography. The criteria for suspicion of renovascular disease were drug-refractory hypertension (blood pressure > 160/95 mm Hg despite administration of 2 classes of antihypertensive drugs), worsening of previously well-controlled hypertension, "de novo" hypertension established in patients older than 45 y, hypertension in patients with abdominal bruit, hypertension associated with atherosclerotic disease elsewhere, or hypertension in patients with otherwise unexplained mild renal insufficiency. The protocol was approved by the Hospital Ethical Committee for Studies in Humans, and informed consent was obtained from all patients.

Received Sep. 20, 1999; revision accepted Dec. 29, 1999.

For correspondence or reprints contact: Jaap J. Beutler, MD, PhD, Department of Nephrology and Hypertension, University Medical Center Utrecht, Rm. F03.226, P.O. Box 85500, 3508 GA Utrecht, The Netherlands.

Protocol

To avoid drug interference, aspirin renography was performed at least 5 d after captopril renography. Therapeutic use of angiotensin-converting enzyme (ACE) inhibitors and nonsteroidal anti-inflammatory drugs was discontinued at least 5 d and 14 d, respectively, before the first renographic study. Patients were allowed to eat a light breakfast and were given 500 mL water 1 h before the investigation to induce sufficient diuresis during scanning. Either 25 mg captopril or 20 mg aspirin per kilogram of body weight were administered orally 1 h before renal scintigraphy. Blood pressure was measured before the administration of the drugs and 1 h later. The aspirin regimen was similar to that of Imanishi et al. (*12*) in patients with unilateral RAS. At this dose, aspirin strongly decreases prostaglandin-E_2 in renal venous plasma obtained from poststenotic and nonstenotic kidneys within 45 min after ingestion (*12*).

Renography was performed using a gamma camera with a large field of view, a low-energy parallel-hole collimator, and computerized data acquisition. After intravenous injection of 50 MBq ^{99m}Tc-MAG3 (Mallinckrodt Medical, Petten, The Netherlands), sequential timed-image data in a 64 × 64 matrix were recorded on a computer: 3-s frames during the first 3 min, followed by 15-s frames (in total, 20 min). Time zero was defined as the time at which the radiopharmaceutical reached the kidneys. Regions of interest and perirenal background regions were assigned for each kidney. A time–activity curve was obtained. The following variables were evaluated: the fractional contribution of each kidney to the total renal uptake measured in the second minute, the time to peak activity (Tmax) for each kidney, and the activity in the cortex at 20 min as a percentage of the activity at Tmax (retention). The time–activity curves were interpreted according to the consensus criteria of Nally et al. (*17*). The renogram was considered to indicate probable RAS if the relative uptake in 1 of the kidneys was less than 40% or if the Tmax in 1 or both kidneys was at least 6 min.

Intra-arterial digital subtraction angiography was performed within 1 mo after the last renographic study using standard techniques. A reduction in renal artery diameter of 50% or more, as assessed in a consensus reading by 2 independent observers, was considered to represent significant RAS. The observers were not informed about the results of the renographic studies.

Statistical Analysis

Tracer uptake and time–activity curves were evaluated separately for each kidney. In patients in whom angiography showed unilateral RAS, the poststenotic kidney was denoted the reference kidney and the other kidney was denoted the contralateral kidney. In patients with significant bilateral RAS, the kidney behind the most severe stenosis was considered the reference kidney. In patients without RAS, the kidney with the least MAG3 uptake during captopril renography was considered the reference kidney. Data are presented as mean ± SEM. Paired *t* tests were used to evaluate differences between reference and contralateral kidneys and between captopril and aspirin renography. A χ^2 test was used to determine differences in sensitivity and specificity between the 2 renographic methods.

RESULTS

Angiographic Findings and Clinical Characteristics

Of the 75 patients enrolled, 34 had unilateral stenosis (including 9 patients with unilateral occlusion) and 17 had bilateral stenosis (including 6 patients with unilateral stenosis and contralateral occlusion). Of the remaining 24 patients, 20 had bilateral normal arteries, 2 had moderate (40%) unilateral stenosis, and 2 had a single kidney, in 1 case with 40% stenosis.

The clinical characteristics of the patients and the causes of their stenosis are listed in Table 1. Mean age was similar among the groups, and most of the patients were men. Mean plasma creatinine was highest in the patients with bilateral RAS, intermediate in the patients with unilateral RAS, and lowest in the patients without RAS. Plasma creatinine differed significantly among all 3 groups.

Renographic Findings

In the patients without RAS, the kidney for which the captopril renogram showed the lowest MAG3 uptake was denoted the reference kidney (Table 2). The time to peak activity and the retention in these kidneys were not different from measurements in the contralateral kidneys. No differences existed between the results for captopril and aspirin renography.

In the patients with significant RAS, the kidney with the most severe stenosis on angiography was denoted the reference kidney. MAG3 uptake in captopril renography was significantly less than in the contralateral kidney (Table 2). In 10 patients, uptake in the reference kidney was less than 15%. This value was found only with both captopril and aspirin renography, not with only 1 of the techniques. Sixteen patients showed accumulation curves, i.e., activity accumulation without evidence of an excretory phase, within 20 min. In 4 patients, these curves were found during both types of renography; in 6, only during captopril renography; and in 6 others, only during aspirin renography. Evaluation of the time to peak activity and the retention data for the remaining 25 patients is given in Table 2. Both time to peak activity and 20-min retention were significantly greater in the reference kidney during both captopril renography and aspirin renography ($P < 0.05$). The findings for the 2 types of renography were comparable.

TABLE 1
Patient Characteristics

Characteristic	RAS		No RAS
	Unilateral	Bilateral	
No. of patients	34	17	24
Mean age ± SD (y)	56 ± 3	66 ± 2	53 ± 3
No. of men	22	10	19
Mean plasma creatinine level ± SD (μmol/L)	127 ± 14	167 ± 16*	102 ± 12†
Etiology of stenosis			
Atherosclerotic	26	16	
Fibromuscular	8	1	

*Significantly ($P < 0.01$) different from unilateral RAS.
†Significantly ($P < 0.02$) different from unilateral and bilateral RAS.

TABLE 2
Time–Activity Curve Characteristics

Characteristic	Uptake (%)		Tmax (s)		Retention (%)	
	Captopril	Aspirin	Captopril	Aspirin	Captopril	Aspirin
No RAS						
Reference kidney	46 ± 0.9	47 ± 0.9	306 ± 50.0	289 ± 45.6	39 ± 4.9	47 ± 5.4
Contralateral kidney	54 ± 0.9*	53 ± 0.9*	286 ± 49.1	235 ± 14.9	38 ± 5.5	41 ± 5.0
RAS						
Reference kidney	41 ± 2.2	41 ± 2.2	306 ± 24.0	360 ± 31.1	53 ± 4.5	57 ± 3.4
Contralateral kidney	59 ± 2.2*	59 ± 2.2*	264 ± 31.8†	276 ± 33.8†	47 ± 5.1†	47 ± 4.9†

*$P < 0.0001$ between contralateral and reference kidney.
†$P < 0.05$ between contralateral and reference kidney.
Tmax = time to peak activity; Retention = activity at 20 min as percentage of maximal activity.
Patients with unilateral occlusion or accumulation curves without excretory phase were not included in this evaluation. Data are expressed as mean ± SEM. No significant difference existed between captopril and aspirin renographies.

Renography and Detection of RAS

Of the 51 cases of RAS, 44 were detected by aspirin renography (sensitivity, 86%) and 45 were detected by captopril renography (sensitivity, 88%) (Table 3). The difference was not significant. In 2 of the 6 patients in whom RAS was not detected by captopril renography, the condition was diagnosed correctly by aspirin renography. Conversely, 3 of the 7 cases missed by aspirin renography were detected by captopril renography. When the results of sequential aspirin and captopril renography were combined, the sensitivity improved to 92% (47/51 patients). Blood pressure in these 51 patients changed from 181/103 ± 5/3 mm Hg to 164/95 ± 4/3 mm Hg during captopril renography ($P <$ 0.001) and from 179/99 ± 4/2 mm Hg to 173/98 ± 4/2 mm Hg during aspirin renography ($P < 0.01$). The decrease was slightly but significantly ($P < 0.001$) larger during captopril renography (17/8 ± 3/2 mm Hg) than during aspirin renography (6/2 ± 2/1 mm Hg). Hypotension (systolic blood pressure < 120 mm Hg) did not occur.

Subgroup analysis showed that the sensitivity for detecting at least 1 abnormally perfused kidney was similar in patients with bilateral RAS and patients with unilateral RAS, but the sensitivity for detecting 2 abnormal kidneys was much lower in patients with bilateral RAS (Table 3). Again, no differences were seen between captopril and aspirin renography.

Subgroup analysis of patients with renal dysfunction (plasma creatinine > 120 μmol/l) also revealed similar sensitivity for captopril renography and aspirin renography (Table 4).

Whereas 50% angiographic stenosis was considered significant in the above evaluation, other investigators have accepted higher margins (*3,13,14*). We therefore also grouped patients with unilateral or bilateral RAS of 50%–75% and patients with unilateral or bilateral RAS greater than 75% (Table 4). For the patients with unilateral stenosis, the detection sensitivity of renography was not significantly better when a higher margin was used. Again, no difference existed between captopril and aspirin renography. The numbers for bilateral stenosis were too small to allow meaningful evaluation.

Captopril renography and aspirin renography were normal in, respectively, 18 and 20 of the 24 patients without RAS (specificity, 75% and 83%; not significant). Hypotension in response to the administration of captopril, a well known cause of false-positive scintigraphy results, was not observed. In the 6 patients with a false-positive result, the fall in blood pressure tended to be greater (28/12 ± 9/6 mm Hg) than that observed in the other patients of this group (8/5 ± 5/2 mm Hg), but the difference was not significant.

DISCUSSION

This prospective study shows that aspirin renography and captopril renography are equally sensitive for identifying

TABLE 3
Sensitivities of Captopril and Aspirin Renographies to Identify RAS

Category	No. of patients	No. with positive findings		Sensitivity (%)	
		Captopril renography	Aspirin renography	Captopril renography	Aspirin renography
No. of patients	51	45	44	88	86
Unilateral RAS	34	30	28	88	82
Bilateral RAS	17	15	16	88	94
Correct identification of bilateral RAS		5	6	29	35

TABLE 4
Subgroup Analysis of Sensitivity of Renography to Identify RAS

Finding	Unilateral			Bilateral		
	No. of patients	Captopril (%)	Aspirin (%)	No. of patients	Captopril (%)	Aspirin (%)
Plasma creatinine >120 μmol/L	10	100	90	12	92	100
Stenosis 50%–75%	13	85	77	2	100	100
Stenosis ≥75%	33	88	88	3	100	100

RAS in patients with unilateral or bilateral renal vascular disease. For captopril renography, the sensitivity, approximately 88%, is in the range reported in the literature (*11,14,18*). For aspirin renography, such numbers are not yet available.

That captopril enhances the sensitivity of renography for detecting RAS is well established (*11,14,18–21*). Optimally, one should compare captopril-enhanced renography with baseline renography, but this comparison will improve only the specificity, not the sensitivity, of the method (*11,18,22*). Our primary question was whether aspirin would further increase the sensitivity. Therefore, we did not obtain baseline renograms but directly compared aspirin renography with captopril renography. Because aspirin and captopril yielded roughly similar results, we can conclude that aspirin indeed enhances the sensitivity of renography as a detection method for RAS, but apparently not more than captopril does.

The rationale for the idea that aspirin may also improve the sensitivity of renography is the increased dependence of the circulation of stenotic kidneys on prostaglandins. In the poststenotic kidney, angiotensin II levels are elevated, causing constriction predominantly in the postglomerular arteriole (*23,24*). The preglomerular arteriole is kept open by increased local levels of vasodilating prostaglandins (*25,26*). Aspirin, which inhibits prostaglandin synthesis, caused preglomerular vasoconstriction, with the double effect of decreasing renal blood flow and decreasing glomerular capillary pressure and filtration rate (*27*). These changes also occurred in the contralateral kidney, but the preglomerular resistance, estimated indirectly (*28*), increased to a significantly higher level in the part of the kidney behind the stenosis (*27*).

Captopril, by releasing the increased postglomerular vasoconstriction, also decreases glomerular capillary hydraulic pressure and filtration rate (*19–21,29–34*) in the poststenotic kidney. However, in contrast to aspirin, captopril does not decrease renal blood flow (*21,29–34*) and therefore will not decrease tubular tracer delivery. On the other hand, captopril may decrease the efficacy of tubular extraction, as has been shown for ^{131}I-hippurate in the poststenotic kidney in humans (*30*) and dogs (*21*) with unilateral RAS. Furthermore, captopril also increases blood flow to the contralateral kidney (*29–34*). The net effect of these complex changes is that captopril has little effect on the difference in uptake of a tubular radiotracer between poststenotic and normal kidneys (*11,18,20*). Because aspirin decreases both glomerular filtration rate and renal blood flow, one might expect that aspirin, compared with captopril, would increase the difference in uptake of the tubularly secreted MAG3 between stenotic and nonstenotic (or less stenotic) kidneys. Because this expectation was not the case, we have to assume that the net effects of aspirin and captopril on the extraction ratios were not different. Notably, aspirin can also lower blood flow to the contralateral kidney (*27*). Furthermore, we cannot exclude that aspirin, while decreasing renal blood flow, can increase the extraction efficacy of tubular radiotracer (*35*).

Both aspirin and captopril lower glomerular capillary pressure and filtration. The latter determines washout of tracer taken up by the kidney and, thus, time to peak activity and residual activity (*11,21*) in the time–activity curves. Whether suppression of glomerular filtration in the poststenotic kidney is stronger for prostaglandin synthesis inhibition or for ACE inhibition has not been comparatively studied. Of possible relevance may be the ability of captopril, in particular in patients with RAS, to lower blood pressure, which further decreases glomerular filtration in the kidney with RAS (*18*). Indeed, the blood pressure during captopril renography was somewhat lower than during aspirin renography, although no hypotension occurred. Aspirin, on the other hand, increases fluid and salt reabsorption, specifically in the hypoperfused kidney (*36*), which will also oppose washout of extracted radiotracer. As it is, we found no significant difference in time–activity curves after aspirin or captopril in both poststenotic and contralateral kidneys. We observed some numeric difference in time to peak activity and retention in favor of aspirin renography, but the sensitivity of these parameters for identifying RAS was not better than for captopril. Thus, we have to conclude that the net effects of aspirin on tracer clearance are similar to those of captopril.

A reasonable presumption is that captopril renography will perform worse in patients with lesser degrees of RAS, because the dependency of the renal circulation on angiotensin II will be less. In patients with bilateral RAS, the reliability to detect both stenoses is also relatively low (*13–16*), probably because sodium retention diminishes the angiotensin dependency of the circulation in (at least) 1 kidney (*37*). From a clinical viewpoint, to see whether aspirin renography would perform better under these specific conditions would be particularly useful. Indeed, it was specifically in patients with moderate unilateral RAS that a

preliminary report showed superior sensitivity for aspirin renography (*12*). However, our subgroup analysis did not confirm this idea or show superior results in patients with bilateral stenosis.

The specificity of captopril renography was 75%, which is similar to figures reported by others (*11,18*). However, this finding, because based on a relatively low number of negative results, has to be interpreted with caution. Important in the context of this study is that the specificity of aspirin renography, 83%, was not less. The specificity of renography is known to be particularly low in patients with decreased renal function (*11,18,22*). In view of the intrinsically low tracer passage, it is not surprising that sensitivity as an indicator for RAS is not low and can even be high, such as was found in this study for both captopril and aspirin renography. Under these conditions, if the findings from captopril renography are compatible with RAS, comparison with baseline renography without captopril is advocated to increase the specificity (*11,18,22*). Administration of furosemide to accelerate tracer washout in patients with low glomerular filtration further enhances the accuracy of the test (*38*). Whether these additions also enhance the accuracy of aspirin renography remains to be studied.

Although the average results for aspirin renography and captopril renography were similar, some intraindividual variability occurred, in that in a few cases only 1 of the 2 techniques yielded a positive result. Consequently, sensitivity for the detection of RAS increased somewhat when the results of the aspirin and captopril renographies were combined. In some patients, positive renography results or an accumulation curve without an excretory phase was found only after captopril, and in others only after aspirin. Although we cannot exclude that this finding points to some specific pathophysiologic difference between individuals, we tend to ascribe this variability to altered conditions within patients. For example, the ability of volume status to influence the results of renography is well known (*11,17,18*). Further, the modest increase in sensitivity does not seem to permit one to recommend that patients undergo both aspirin and captopril renography. However, worthwhile to study would be whether combined administration of aspirin and captopril can improve the sensitivity of renography. Inhibition of prostaglandin synthesis has been shown to enhance the antiproteinuric effect of ACE inhibition in nephrotic patients (*39*). Although this situation is different from the one we studied, it may be relevant because that interaction is probably based on a more profound suppression of glomerular capillary pressure and filtration rate (*40*).

CONCLUSION

In summary, in this group with a high prevalence of RAS, we found that aspirin renography and captopril renography were equally sensitive for identifying patients with RAS. We could not confirm earlier preliminary data suggesting greater sensitivity for aspirin renography. To improve the sensitivity, it may be worthwhile to combine aspirin and captopril renography in future studies.

ACKNOWLEDGMENT

This study was supported by the Dutch Kidney Foundation, grant C95.1516.

REFERENCES

1. Bech K, Hilden T. The frequency of secondary hypertension. *Acta Med Scand.* 1975;197:65–69.
2. Van Velzer DA, Burge CH, Morris GC. Arteriosclerotic narrowing of renal arteries associated with hypertension. *AJR.* 1961;86:807–818.
3. Derkx FHM, Schalekamp MADH. Renal artery stenosis and hypertension. *Lancet.* 1994;344:237–239.
4. Apple RG, Bleyer AJ, Reavis S, Hansen KJ. Renovascular disease in older patients beginning renal replacement therapy. *Kidney Int.* 1995;48:171–176.
5. Mailloux LU, Napolitano B, Belluci AG, Vernace M, Wilkes BM, Mossey RT. Renal vascular disease causing end-stage renal disease, incidence, clinical correlates, and outcomes: a 20-year clinical experience. *Am J Kidney Dis.* 1994;24:622–629.
6. Scoble JE, Maher ER, Hamilton G, Dick R, Sweny P, Moorhead JF. Atherosclerotic renovascular disease causing renal impairment: a case for treatment. *Clin Nephrol.* 1989;31:119–122.
7. Jensen G, Zachrisson BF, Delin K, Volkmann R, Aurell M. Treatment of renovascular hypertension: one year results of renal angioplasty. *Kidney Int.* 1995;48:1936–1945.
8. Ven van de PJG, Beutler JJ, Kaatee R, et al. Transluminal vascular stent for ostial atherosclerotic renal artery stenosis. *Lancet.* 1995;346;672–674.
9. Harden PN, MacLeod MJ, Rodger RSC, et al. Effect of renal-artery stenting on progression of renovascular renal failure. *Lancet.* 1997;349:1133–1136.
10. Rudnick MR, Berns JS, Cohen RM, Goldfarb S. Nephrotoxic risks of renal angiography: contrast media-associated nephrotoxicity and atheroembolism—a critical review. *Am J Kidney Dis.* 1994;24:713–727.
11. Prigent A. The diagnosis of renovascular hypertension: the role of captopril renal scintigraphy and related issues. *Eur J Nucl Med.* 1993;20:625–644.
12. Imanishi M, Yano M, Hayashida K, et al. Aspirin renography to detect unilateral renovascular hypertension. *Kidney Int.* 1994;45:1170–1176.
13. Mann SJ, Pickering TG, Sos TA, et al. Captopril renography in the diagnosis of renal artery stenosis: accuracy and limitations. *Am J Med.* 1991;90:30–40.
14. Fommei E, Ghione S, Hilson AJW, et al. Captopril radionuclide test in renovascular hypertension: a European multicenter study. *Eur J Nucl Med.* 1993;20:617–662.
15. Scoble JE, McClean A, Stansby G, Hamilton G, Sweny P, Hilson AJW. The use of captopril-DTPA scanning in the diagnosis of atherosclerotic renal artery stenosis in patients with impaired renal function. *Am J Hypertens.* 1991;4(suppl 12):721S–723S.
16. Mittal BR, Kumar P, Arora P, et al. Role of captopril renography in the diagnosis of renovascular hypertension. *Am J Kidney Dis.* 1996;28:209–213.
17. Nally JV Jr, Chen C, Fine E, et al. Diagnostic criteria of renovascular hypertension with captopril renography: a consensus statement. *Am J Hypertens.* 1991;4(suppl 12):749S–752S.
18. Taylor A, Nally J, Aurell M, et al. Consensus report on ACE inhibitor renography for detecting renovascular hypertension. *J Nucl Med.* 1996;37:1876–1882.
19. Geyskes GG, Oei HY, Puylaert CBAJ, Dorhout Mees EJ. Renography with captopril: changes in a patient with hypertension and unilateral renal artery stenosis. *Arch Intern Med.* 1986;146:1705–1708.
20. Geyskes GG, Oei HY, Puylaert CABJ, Dorhout Mees EJ. Renovascular hypertension identified by captopril-induced changes in the renogram. *Hypertension.* 1987;9:451–458.
21. Jonker GJ, Zeeuw de D, Huisman RM, Piers DB, Beekhuis H, Hem van der GK. Angiotensin converting enzyme inhibition improves diagnostic procedures for renovascular hypertension in dogs. *Hypertension.* 1988;12:411–419.
22. Bourgoignie JJ, Rubbert K, Sfakianakis GN. Angiotensin-converting enzyme-inhibited renography for the diagnosis of ischemic kidneys. *Am J Kidney Dis.* 1994;24:665–673.
23. Hall JE, Guyton AC, Jackson TE, Coleman TG, Lohmeier TT, Trippodo NC. Control of glomerular filtration rate by renin-angiotensin system. *Am J Physiol.* 1997;233:F366–F372.
24. Frega NS, Davalos M, Leaf A. Effect of endogenous angiotensin on the efferent arteriole in the rat kidney. *Kidney Int.* 1980;18:323–327.

25. Romero JC, Strong CG. The effect of indomethacin blockade of prostaglandin synthesis on blood pressure of normal rabbits and rabbits with renovascular hypertension. *Circ Res.* 1977;40:35–41.
26. Olsen ME, Hall JE, Montani J-P, Cornell JE. Interaction between renal prostaglandins and angiotensin I in controlling glomerular filtration in the dog. *Clin Sci.* 1987;72:429–436.
27. Milot A, Lambert R, Lebel M, Cusson JR, Larochelle P. Prostaglandins and renal function in hypertensive patients with unilateral renal artery stenosis and patients with essential hypertension. *J Hypertens.* 1996;14:765–771.
28. Kimura G, London GE, Safar ME, Kuramochi M, Omae T. Glomerular hypertension in renovascular hypertensive patients. *Kidney Int.* 1991;39:966–972.
29. Ploth DW. Angiotensin-dependent renal mechanisms in two-kidney one-clip renal vascular hypertension. *Am J Physiol.* 1983;245:F131–F141.
30. Wenting GJ, Tan-Tjiong HL, Derkx FHM, de Bruyn JHB, Man in't Veld AJ, Schalekamp MADH. Split renal function after captopril in unilateral renal artery stenosis. *Br Med J.* 1984;288:886–890.
31. Nally JV, Clarke HS, Grecos GP, et al. Effect of captopril on ^{99m}Tc-diethylenetriaminepentaacetic acid renograms in two-kidney, one clip hypertension. *Hypertension.* 1986;8:685–693.
32. Tamaki N, Alpert NM, Rabito CA, Barlai-Kovach M, Correia JA, Strauss HW. The effect of captopril on renal blood flow in renal artery stenosis assessed by positron tomography with rubidium-82. *Hypertension.* 1988;11:217–222.
33. Anderson WP, Denton KM, Woods RL, Alcorn D. Angiotensin II and the maintenance of GFR and renal blood flow during renal arterial narrowing. *Kidney Int.* 1990;38:S109–S113.
34. Miyamori I, Yasuhara S, Matsubara T, Takasaki H, Takeda R. Comparative effects of captopril and nifedipine on split renal function in renovascular hypertension. *Am J Hypertens.* 1988;1:359–363.
35. Muther RS, Potter DM, Bennet WM. Aspirin-induced depression of glomerular filtration rate in normal humans: role of sodium balance. *Ann Intern Med.* 1981;94:317–321.
36. Raymond KH, Lifschitz MD. Effect of prostaglandins on renal salt and water excretion. *Am J Med.* 1986;80(suppl 1A):22–33.
37. Laragh JH. Renovascular hypertension: a paradigm for all hypertension. *J Hypertens.* 1986;4(suppl 4):S79–S88.
38. Erbsloh-Möller B, Dumas A, Roth D, Sfakianakis GN, Bourgoignie JJ. Furosemide ^{131}I-hippuran renography after angiotensin-converting enzyme inhibition for the diagnosis of renovascular hypertension. *Am J Med.* 1991;90:23–29.
39. Heeg JE, de Jong PE, Vriesendorp R, de Zeeuw D. Additive antiproteinuric effect of the NSAID indomethacin and the ACE inhibitor lisinopril. *Am J Nephrol.* 1990;10(suppl 1):94–97.
40. Heeg JE, de Jong PE, de Zeeuw D. Additive antiproteinuric effect of angiotensin converting enzyme and non-steroidal anti-inflammatory drug therapy: a clue to the mechanism of action. *Clin Sci.* 1991;81:367–372.