

Hypotensive Response to Captopril: A Potential Pitfall of Scintigraphic Assessment for Renal Artery Stenosis

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A characteristic pattern seen on captopril renography is described that is due to systemic hypotensive response. Most patients with these findings on captopril renography do not receive renal artery angiograms in our clinic because it is usually recognized. However, this pattern has received little attention in the medical literature and may be misinterpreted as being due to physiologically significant renal artery hypertension. **Methods:** Over the last 3 y, renal artery angiograms were performed on three patients with systemic hypotensive response pattern on captopril renography. This allowed a unique opportunity to correlate the results of the captopril renogram with the renal artery angiograms in this patient population. Captopril renography was performed with a glomerular filtration agent, diethylenetriamine pentaacetic acid (DTPA), and a tubular agent, o-iodohipurate (OIH). **Results:** Renal artery angiograms showed no evidence of renal artery stenosis in three patients with systemic hypotensive response pattern on captopril renography. Systemic hypotension on captopril renograms results in preserved uptake of both DTPA and OIH and hyperconcentration in the cortex and collecting system. **Conclusion:** The systemic hypotensive response pattern seen on captopril renography is a distinctive pattern that does not represent physiologically significant renal artery stenosis.

Key Words: hypertension; kidney; captopril; radionuclide studies; renal artery stenosis

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A small subset of hypertensive patients have renovascular hypertension caused by a stenotic renal artery. However, not all patients with renal artery stenosis have renovascular hypertension. Captopril renography is a common examination used to evaluate the physiological significance of renal artery stenosis (RAS) (1–3). Our protocol determines RAS to be physiologically significant when there is captopril-induced disruption of the normal relationship between tubular function and glomerular filtration (4). A physiologi-

cally significant RAS must demonstrate a captopril-induced drop in glomerular filtration, as shown by ^{99m}Tc -diethylenetriamine pentaacetic acid (DTPA), in the face of normal or increased blood flow, normal uptake of tubular agents (as indicated by scintigraphic 2-min cortical counting or plasma disappearance curves) and by increased retention of tubular agents.

We describe a pattern seen on captopril renography in which there is slower accumulation and retention of DTPA and o-iodohipurate (OIH) with preserved relative uptake of both agents and prolonged retention in the cortex and collecting system. The pattern is due to systemic hypotension that occurs after captopril administration but may be misinterpreted as being positive for RAS if the reader is unfamiliar with this finding or if only a single agent is used to perform captopril renography. This pattern has been seen 11 times in the last 10 y (approximately 950 total cases) and was previously described in a renal transplant patient (4). This phenomenon has not been seen with a mean arterial blood pressure drop of less than 20 mm Hg. Renal angiography is typically not performed in these patients because this is a recognized pattern in our clinic. We present three patients who did undergo angiography for a variety of reasons. All three had no angiographic evidence of RAS in the kidneys showing this pattern on captopril renography.

MATERIALS AND METHODS

Over the last 3 y, three patients with a characteristic systemic hypotensive response pattern on captopril renography underwent renal angiography. Our protocol for captopril renography begins with a captopril challenge scan (4). All patients are well hydrated before the procedure. Oral captopril (0.7 mg/kg) is administered. The patient is monitored in the supine position for 1 h with serial blood pressure measurements taken by an automatic blood pressure monitoring system every 10 min.

All imaging is performed with a large-field-of-view gamma camera equipped a medium-energy collimator. This is interfaced to a standard nuclear medicine computer. At 1 h, a DTPA scan is performed with 740 MBq (20 mCi) ^{99m}Tc -labeled DTPA administered intravenously. A flow study at 2 s/frame followed by 1 min/frame serial images for 27 min is performed. The patients are then injected with 11.1 MBq (300 μCi) ^{131}I -OIH, and images were

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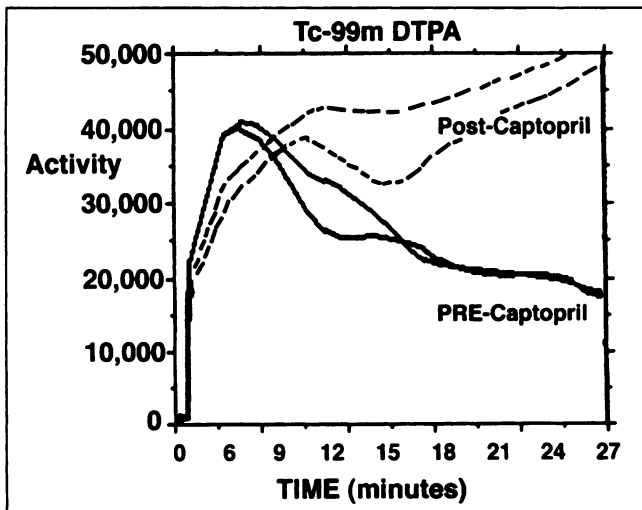


FIGURE 1. DTPA curves show progressive increase of radiotracer in both kidneys after captopril administration. Precaptopril study is normal.

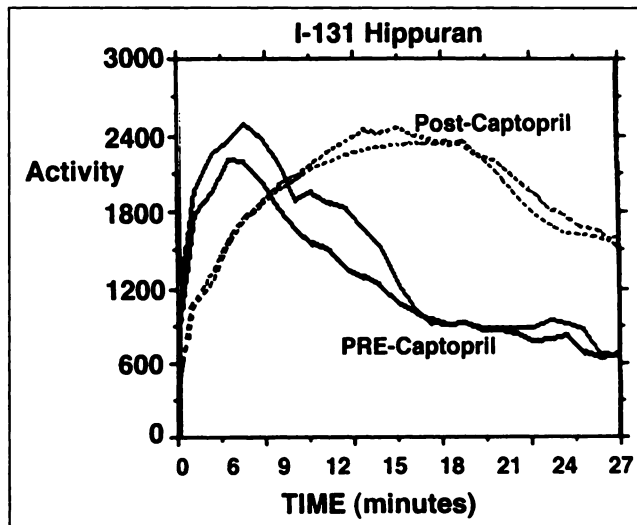


FIGURE 3. OIH curves show progressive accumulation of radiotracer in both kidneys with minimal drainage bilaterally after captopril administration. Precaptopril OIH study is normal.

obtained at 1 min/frame for 27 min. A blood sample is drawn 44 min after OIH administration (72 min after DTPA injection), and another blood sample is taken 3 h after injection of DTPA. The two blood samples are immediately used to calculate glomerular filtration rate (GFR). After allowing 24 h for the ^{99m}Tc to decay, the first blood sample is used to calculate effective renal plasma flow (ERPF). The following day, the entire series of images is repeated without captopril, unless the postcaptopril series is normal.

RESULTS

Most patients with this systemic hypotension response pattern seen on captopril renography do not then undergo angiography. The three patients in this study did for a variety of reasons, as discussed below. This allowed us to correlate the results of the captopril renograms with the renal angiograms. In all three patients, the kidneys that showed evidence of

this distinctive pattern on the captopril renogram demonstrated no evidence of RAS on renal artery angiography.

Case 1

A 65-y-old woman presented to her primary care physician with a 2-y history of poorly controlled hypertension while taking antihypertensives. Physical examination revealed an abdominal bruit that radiated to the right upper quadrant. Her creatinine was 1.5. Captopril renography was subsequently recommended to evaluate the patient for physiologically significant RAS.

At the time of captopril renography, the patient's blood pressure dropped from a baseline mean arterial pressure of 107 mm Hg to a postcaptopril mean arterial pressure of 74 mm Hg at the time of imaging. The study was initially interpreted as bilateral physiologically significant RAS, on the basis of the cortical retention of OIH, and the recommen-

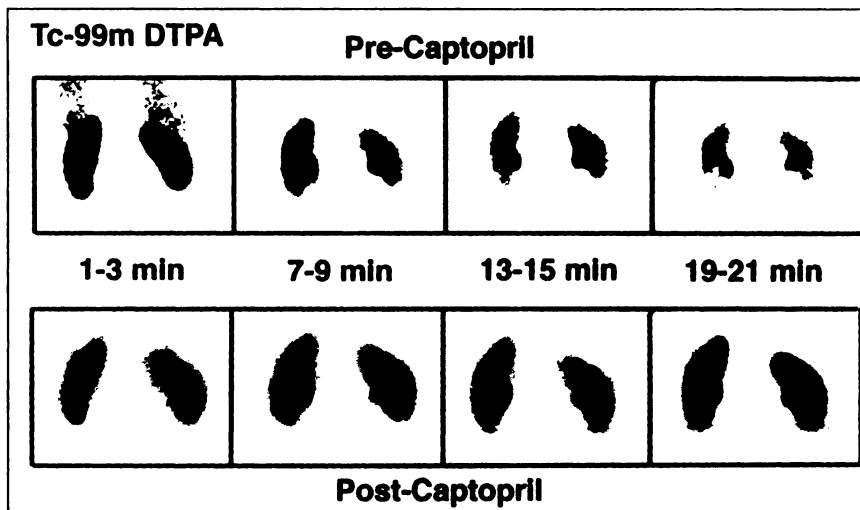


FIGURE 2. DTPA images demonstrate progressive accumulation of DTPA in both kidneys after captopril administration.

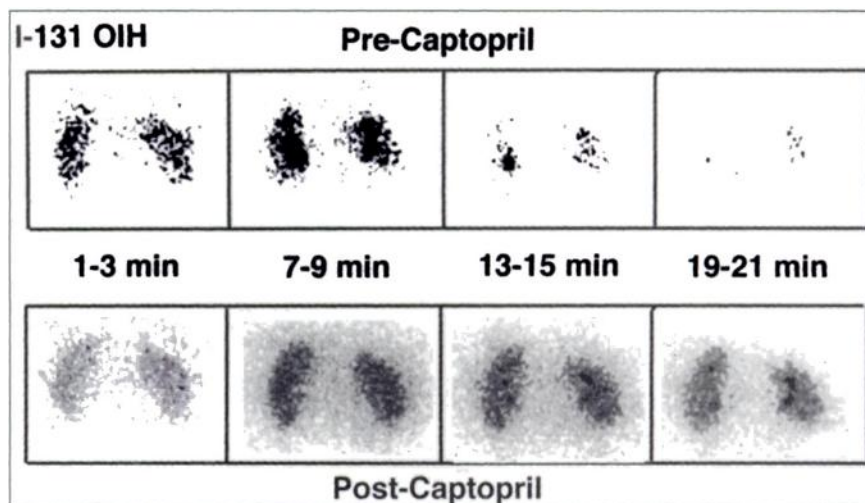


FIGURE 4. OIH images demonstrate progressive accumulation of radiotracer in both kidneys with little drainage bilaterally after captopril administration.

dation was made for a renal angiogram. However, reevaluation of the examination by one of the authors revealed that both DTPA and OIH progressively accumulated in the renal cortex and collecting systems (Figs. 1–4). This is a pattern of systemic hypotension effect and not RAS. The clinicians and the patient decided to proceed with the renal angiogram to definitively exclude the question of RAS, despite this new interpretation. The renal angiogram showed normal renal arteries bilaterally (Figs. 5 and 6).

Case 2

The second case is a 5-y-old girl with a history of poorly controlled hypertension and a creatinine of 1.1. Captopril renography was performed to evaluate for physiologically significant RAS (Fig. 7). The patient's blood pressure decreased from a baseline mean arterial pressure of 125 mm Hg (156/114 mm Hg) to a postcaptopril mean arterial pressure of 100 mm Hg (131/85 mm Hg) at the time of imaging. The study was interpreted as demonstrating physiologically significant RAS that involved the left kidney. Captopril caused DTPA uptake to decrease, while OIH uptake was maintained with poor clearance. The effect of



FIGURE 5. Normal renal arteries are seen bilaterally during aortography.

systemic hypotension without RAS was demonstrated in the right kidney. The systemic hypotension caused both DTPA and OIH to progressively accumulate in the right renal cortex and collecting system. The patient then underwent renal angiography, which confirmed the left RAS and a normal right renal artery (Fig. 8). Splenic to renal artery bypass was performed on the left RAS, and the patient has been normotensive for 3 y without medication.

Case 3

A third case is a 22-mo-old boy with neurofibromatosis type I and uncontrolled hypertension. His creatinine was 0.9. During captopril renography, the patient's blood pressure decreased 31 mm Hg from a mean arterial pressure of 121 to 91 mm Hg, after the administration of captopril. The precaptopril DTPA scan demonstrated mild asymmetry in uptake (Fig. 9). Both kidneys showed decreased intrarenal transit with cortical retention of DTPA. The precaptopril OIH scan demonstrated similar findings to the DTPA scan, with somewhat better bilateral clearance. The postcaptopril DTPA scan demonstrated marked reduction of flow and function on the right. This effect was nonuniform and suggestive of two renal arteries. Progressive accumulation of DTPA was demonstrated on the left. The postcaptopril OIH scan showed progressive accumulation of radiotracer in both kidneys. These findings were interpreted as physiologically significant RAS on the right, along with a systemic hypotension pattern without RAS on the left. After captopril administration, RAS caused DTPA uptake to decrease on the right, while OIH uptake was maintained with poor clearance. Systemic hypotension caused both DTPA and OIH to progressively accumulate in the cortex and collecting system of the left kidney.

The renal angiogram demonstrated two renal arteries bilaterally (Fig. 10). The larger and more superior right renal artery showed a 90%–95% stenosis at its origin with poststenotic dilatation. The smaller accessory right renal

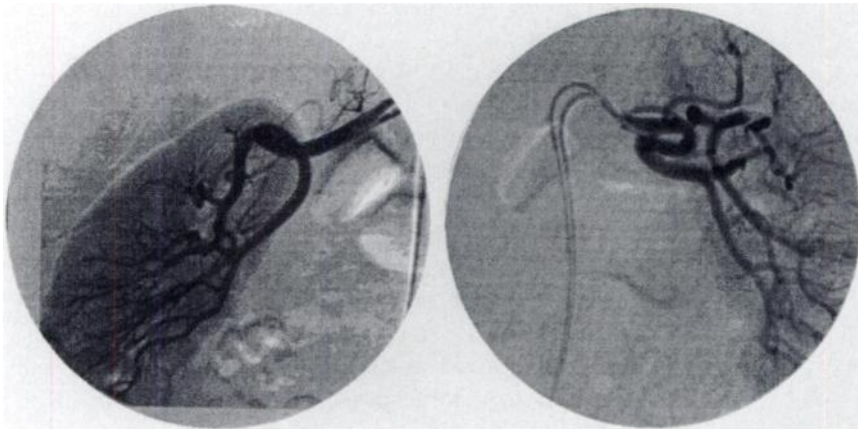


FIGURE 6. Normal renal arteries are demonstrated bilaterally after selective renal artery angiography.

artery supplied the lower pole and showed no stenosis. Both left renal arteries showed no stenoses. Renin measurements were obtained: right renal vein = 54.3 ng/mL/h; left renal vein = 36.6 ng/mL/h; infrarenal inferior vena cava = 48.5 ng/mL/h; suprarenal inferior vena cava = 46.9 ng/mL/h. The patient underwent iliac bypass of the stenosed superior right renal artery. This was complicated by postoperative thrombosis 2 wk after surgery, and the patient then underwent nephrectomy.

DISCUSSION

Although important attempts have been made to standardize the performance and interpretation of angiotensin-converting enzyme inhibitor renography in the literature, many different techniques for performing captopril renography persists (5). The current technique involves precaptopril and postcaptopril DTPA and OIH imaging (4). At our institution, the following criteria indicate a positive study for RAS: (a) decreased uptake of DTPA on postcaptopril

imaging compared with the precaptopril DTPA and (b) preserved uptake of OIH with delayed clearance on postcaptopril imaging. It is this captopril-induced separation of blood flow (OIH) and filtration (DTPA) that we consider the hallmark of physiologically significant RAS.

Captopril renography is somewhat time consuming, and there have been many suggestions of methods to simplify or shorten the procedure. The most common method to shorten the procedure is to eliminate the baseline study and perform the postcaptopril study with only 1 agent. The single agent method most frequently uses a tubular secretion agent, either ^{131}I -OIH or Tc-mercaptoacetyltriglycine (MAG3). If only a single tubular agent (OIH or MAG3) had been used in our three patients, all would have been interpreted as bilateral RAS, because bilateral delay in OIH clearance occurred after captopril administration.

Some investigators have suggested that progressive accumulation of DTPA on the postcaptopril time-activity curve is indicative of a physiologic effect on the kidney and therefore

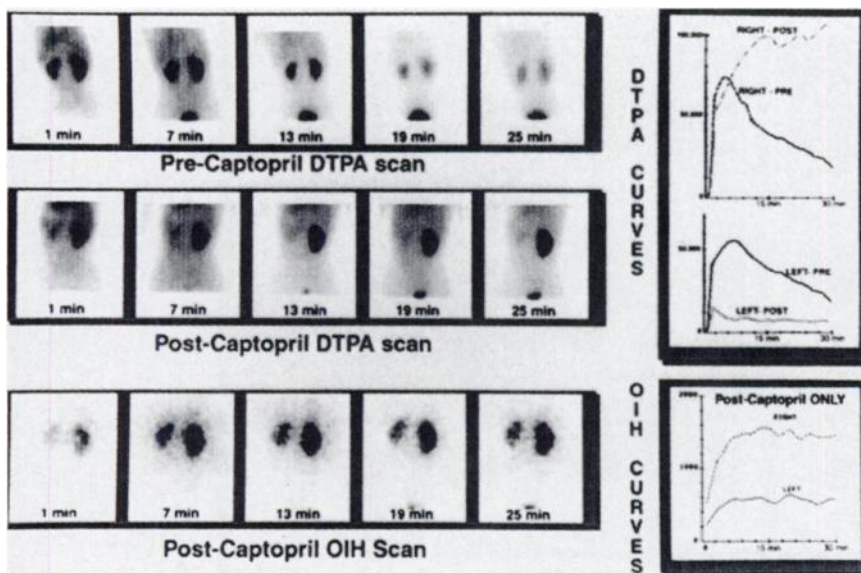


FIGURE 7. Precaptopril findings: DTPA scan demonstrates mildly decreased uptake by left kidney in comparison with right, but scan was otherwise normal (differential function 59% right, 41% left). Baseline OIH precaptopril scan was not performed because of patient intolerance to the procedure (inability to sedate and maintain intravenous access). Postcaptopril findings: DTPA scan demonstrates poor uptake of radiotracer by left kidney and progressive cortical accumulation of radiotracer by right kidney (differential function 81% right, 19% left). OIH scan demonstrates moderately decreased radiotracer uptake on left and progressive accumulation of radiotracer with little drainage bilaterally (differential function 71% right, 29% left).

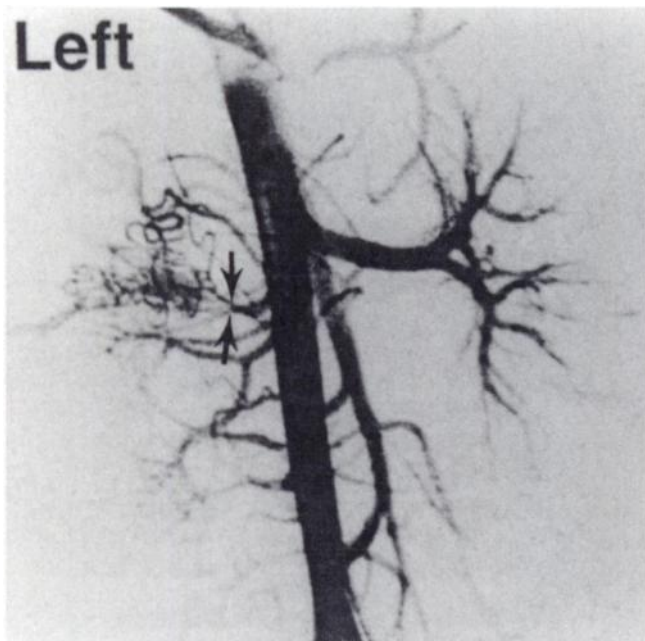


FIGURE 8. Renal angiogram shows complete occlusion of left renal artery (arrows). Tangle of collateral vessels supplied only arterial flow to left kidney. Right renal artery was normal.

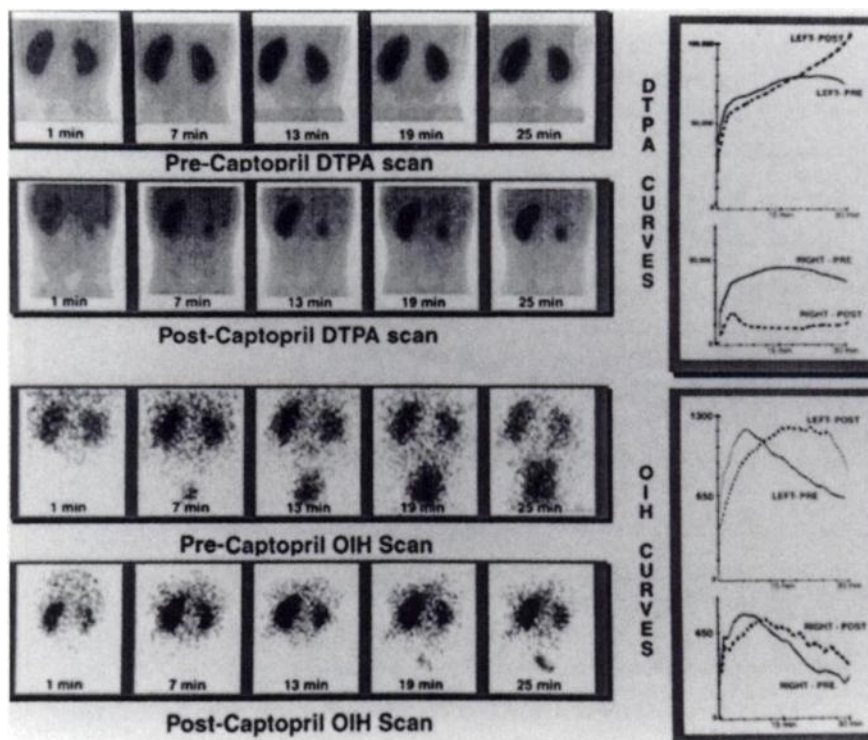
evidence of physiologically significant RAS (6). Application of this criterion to these patients would have incorrectly diagnosed bilateral RAS in all of them. The renal arteries in the first patient were clearly normal, whereas the other two patients had only unilateral RAS.

We have encountered this pattern of progressive cortical

accumulation of both DTPA and OIH on numerous occasions in patients being evaluated for physiologically significant RAS. The drop in mean arterial pressure appears to cause the described changes in normal kidneys. It is unknown exactly what mechanism causes these changes. Although we have performed no experimental testing in this area, one potential hypothesis is that these changes are mediated through an aldosterone/antidiuretic hormone effect, which stimulates hyperconcentration of urine. DTPA imaging clearly shows this effect to be different than a positive captopril effect with RAS. However, DTPA scans alone may not be as sensitive for RAS as OIH studies, and we continue to perform both examinations. Normally, ERPF and GFR are directly related. An increase in one causes an increase in the other. Captopril eliminates this relationship, and this separation of ERPF and GFR is the hallmark of captopril effect. This fact is the reason we continue to monitor both GFR and ERPF using DTPA and OIH, as we have previously described (4). The only other disease state to do this is acute tubular necrosis.

The first case highlights the clinical significance of correctly interpreting this pattern of progressive cortical accumulation of both DTPA and OIH caused by systemic hypotension. An unnecessary renal angiogram could have been avoided if the pattern of systemic hypotension was initially identified. The second and third patients would have undergone angiography because of the unilateral RAS, even if the pattern of systemic hypotension was not correctly diagnosed. However, it is still clinically relevant to identify this pattern so bilateral RAS is not incorrectly diagnosed on

FIGURE 9. Precaptopril findings: DTPA scan demonstrates mild asymmetry in uptake. Both kidneys showed decreased intrarenal transit with cortical retention. OIH scan demonstrates findings similar to those of DTPA scan with somewhat better clearance bilaterally. Postcaptopril findings: DTPA scan demonstrates marked reduction of flow and function on right. This effect was nonuniform and suggestive of two renal arteries. Progressive accumulation of radiotracer was seen on left. OIH scan shows progressive accumulation of radiotracer in both kidneys. Patient's blood pressure decreased 31 mm Hg after administration of captopril. These findings were interpreted as: (a) physiologically significant RAS on right (captopril caused DTPA uptake to decrease, while OIH uptake was maintained with poor clearance) and (b) effect of systemic hypotension without RAS on left (captopril caused both DTPA and OIH to progressively accumulate in cortex).



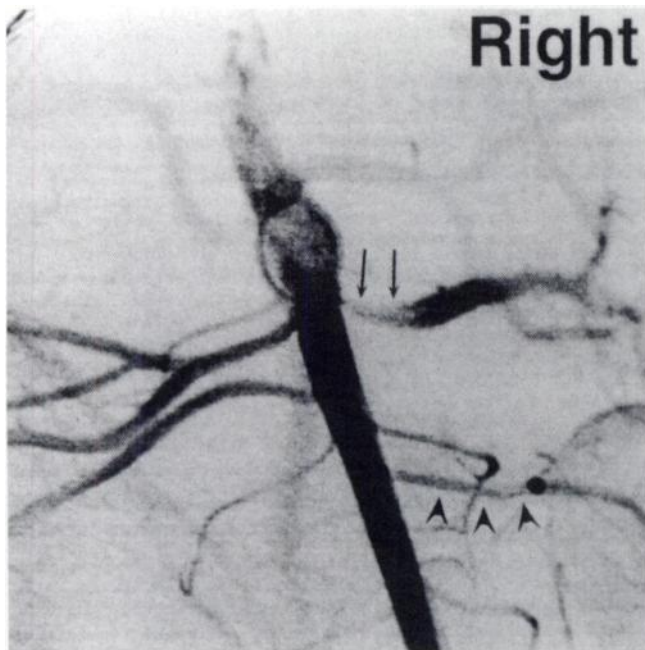


FIGURE 10. Renal angiogram demonstrates two renal arteries bilaterally. Larger and more superior right renal artery shows 90%–95% stenosis at its origin (straight arrows) with poststenotic dilatation. Smaller accessory right renal artery (arrowheads) supplied lower pole and shows no stenosis. Both left renal arteries show no stenoses.

captopril renography. It is important for the angiographer to know which side is responsible for the physiologically significant RAS before the angiogram, so proper therapeutic options can be planned. In addition, bilateral RAS with

physiologically significant disease on one side and insignificant disease on the other is common and unnecessary revascularization should be avoided.

CONCLUSION

We describe a pattern on captopril renography that is due to a systemic hypotensive response (progressive accumulation of both DTPA and OIH). We believe that precaptopril and postcaptopril imaging with both DTPA and OIH allows us to distinguish between the pattern of systemic hypotension and physiologically significant RAS. This pattern would be misinterpreted by single-agent imaging with OIH or MAG3. This pattern would also be misinterpreted if one were to use the criterion of progressive accumulation of DTPA as being consistent with RAS. Most importantly, this pattern should not be interpreted as physiologically significant RAS.

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