

# $^{99m}\text{Tc}$ Diethylenetriaminepentacetic Acid Angiotension-converting Enzyme Inhibitor Renography as Screening Test for Renovascular Hypertension in Unilateral Small Kidney: A Prospective Study

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## Abstract

To know the probability of renal artery stenosis (RAS) in unilateral small kidney and function of the unilateral small kidney, which includes glomerular filtration rate, differential function, uptake, T<sub>max</sub> by  $^{99m}\text{Tc}$  diethylenetriaminepentacetic acid (DTPA) base and  $^{99m}\text{Tc}$  DTPA angiotensin converting enzyme (ACE) inhibition scan. All our patients were subjected to  $^{99m}\text{Tc}$  DTPA ACE inhibition renal scintigraphy. All the patients underwent either computed tomography (CT) angiography and magnetic resonance (MR) angiography was done in those patients in which kidney function test was deranged. Renal angiography was subsequently performed in cases with the suggestion of RAS on CT or MR angiography. The quantitative data was expressed as the arithmetic mean, standard deviation and percentages. The intergroup comparisons for parametric data were done by Student's *t*-test, whereas non-parametric data was compared with Mann-Whitney U-test. The intergroup comparisons were made by paired *t*-test and Wilcoxon sign rank test.  $P < 0.05$  was considered to be significant, and data was analyzed by Statistical package for social sciences (SPSS-20) software. Out of 47 patients, 25 patients were in the low probability group out of which none was positive for RAS on CT/MR angiography. Out of 47 patients, 12 were in the intermediate group out of which none was positive for RAS. Ten, out of 47 patients were suspected of high probability for RAS by ACE inhibition scan out of which 4 were positive for RAS by CT/MR angiography including one with bilateral RAS.  $^{99m}\text{Tc}$  DTPA angiotension-converting enzyme inhibitor renography is a safe, non-invasive, sensitive, specific, and cost-effective test for excluding renovascular hypertension in patients who have normal or nearly normal renal function in unilateral small kidney.

**Keywords:**  $^{99m}\text{Tc}$  diethylenetriaminepentacetic acid angiotension-converting enzyme inhibitor renography, probability of renal artery stenosis, unilateral small kidney

## Introduction

Renal vascular hypertension (RVH) accounts for <1% of cases of secondary hypertension in unselected populations, and is the cause of hypertension in as

many as 30% of cases in selected populations.<sup>[1]</sup> RVH occurs when there is renal artery stenosis (RAS). In older patients, RAS usually is the result of atherosclerosis with increasing luminal narrowing. Fibromuscular dysplasia accounts for approximately 25% of all cases of RVH, and it affects children, young to middle-aged adults, and mostly women under the age of 35 years.<sup>[2]</sup>

Angiotension-converting enzyme inhibitor (ACEI) renography is a safe, non-invasive, sensitive, specific, and cost-effective test for excluding renovascular hypertension in patients who have normal or nearly normal renal function. It can be performed in patients

### Access this article online

#### Quick Response Code:



#### Website:

www.wjnm.org

#### DOI:

10.4103/1450-1147.144815

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who have moderate to high-risk for renovascular hypertension; patients who have severe hypertension; or patients under the age of 30 years or over the age of 55 years who have abrupt or recent onset of hypertension; hypertension that is resistant to medical therapy; abdominal or flank bruits; unexplained azotemia; worsening renal function during therapy with ACEIs; end-organ damage; or occlusive disease in other vascular beds.<sup>[3]</sup>

Accordingly, the role of ACEI renography is to exclude RVH in hypertensive populations and more importantly, to identify patients who are candidates for surgery. The most widely accepted procedure for interpretation of ACEI renography is based on changes in renograms before and after angiotensin converting enzyme (ACE) inhibition.<sup>[4]</sup> In this qualitative grading system, an examination is considered as positive if grade decreases on the postcaptopril scan compared with the baseline study. According to a consensus report, ACEI renography can be categorized as low probability, intermediate probability, and high probability for RVH.<sup>[5]</sup> The sensitivity of the test varies from 83% to 100% and specificity ranges from 62% to 100%, respectively.<sup>[6]</sup> The prospective studies on RAS presenting as unilateral small kidneys are scanty. The present prospective study was undertaken to use renal scintigraphy as a screening test to diagnose RAS in patients presenting with unilateral small kidney.

## **Materials and Methods**

The present study was conducted in the Department of Nuclear Medicine from July 2007 to April 2011. As per hospital policy, informed consent was taken and signed by the patients and referring doctors. The study included 47 patients with diagnosis of unilateral small kidney on ultrasound. All patients had clinical assessments - height, weight, pulse, and blood pressure (BP), laboratory investigations included serum urea, creatinine, uric acid, and urinalysis. All were subjected to baseline and <sup>99m</sup>Tc diethylenetriaminepentacetic acid (DTPA) ACE inhibition renal scintigraphy. All the patients underwent computed tomography (CT) angiography who had normal serum creatinine (<1.5 mg/dl) and magnetic resonance (MR) angiography was performed in those cases who had serum creatinine >1.5 mg/dl. Renal angiography was subsequently performed in cases with the suggestion of RAS on CT or MR angiography.

The probability for renovascular hypertension has been followed according to the consensus report on ACE inhibitor renography for detecting renovascular hypertension.<sup>[5]</sup>

### **Low probability**

Normal findings on ACEI renography indicate a low probability (<10%) for renovascular hypertension. Abnormal baseline findings that improve after ACE inhibition also indicate low probability for renovascular hypertension.

### **Intermediate probability**

Patients with intermediate probability of disease have abnormal baseline findings, but the renogram is unchanged after ACE inhibition.

### **High probability**

The probability is considered as high (>90%) when marked change of the renogram curve occurs after ACE inhibition compared with baseline findings. For DTPA, this change can be quantitated by measuring the change in relative function or absolute individual kidney function.

### **Specific interpretive criteria for DTPA<sup>[5]</sup>**

Reduction in relative uptake >10% after ACEI administration indicates a high probability for renovascular hypertension; on an average, 5-9% indicates intermediate response. High probability is also associated with a 10% decrease in calculated glomerular filtration rate (GFR) of the ipsilateral kidney after ACEI administration. A small poorly functioning kidney (30% uptake) that shows no change after ACEI renography are indicative of intermediate probability for renovascular hypertension.

## **Observation**

Out of the 10 cases in high probability group in <sup>99m</sup>Tc DTPA ACEI scan, 4 (40.0%) were positive for RAS by CT/MR angiography.

All the four positive cases were confirmed by catheter renal angiography.

## **Discussion**

Our study outlines the probability of RAS by <sup>99m</sup>Tc DTPA ACEI scan for small kidney. Twenty-five out of 47 patients were in the low probability group out of which none was positive for RAS on CT/MR angiography. Out of 47 patients, 12 were in the intermediate group out of which none was positive for RAS. Ten out of 47 patients were suspected of high probability. Their differential function and change in GFR was more than 10% by ACE inhibition scan, out of which 4 were positive for RAS by CT/MR angiography including one with bilateral RAS. These four patients were further subjected to catheter

renal angiography and were detected positive for RAS. Thus in high probability group sensitivity was 100% and specificity was 40%. Six (60%) patients in the high probability group showed a false-positive result. All the 6 patients were in the age ranges of 23-60 (mean = 46.3) years. The cause of this false-positivity is not clear, but could be explained on the basis of small renal arteries causing ischemia. However, only two of these six patients were hypertensive [Tables 1 and 2]. We did not study the renal vein renin levels in these patients, which could clarify if high renin levels are present in these patients with false-positive results.

Taylor *et al.* gave the procedure guidelines for patients who are suspected of RAS and categorized them into low, intermediate and high probability.<sup>[7]</sup> In a meta-analysis of diagnostic tests for RAS in patients suspected of having renovascular hypertension using captopril-enhanced scintigraphy in 49 cases (30 males and 19 females) the sensitivity of captopril renal scintigraphy ranged from 58% to 95% and specificity ranged from 17% to 100%.<sup>[8]</sup> Roccatello and Picciotto found the sensitivity of 79.3% and specificity of 70%.<sup>[9]</sup> Abdulsamea *et al.* did a study on 74 children using <sup>99m</sup>Tc MAG3 who had a clinical suspicion of renovascular disease, 12 out of 49 patients who had a low probability for RAS were proven to have RAS on digital subtraction angiography (DSA). Three out of 14 patients who were in the intermediate probability group had RAS on DSA. Nine out of

11 patients who were in high probability group had RAS on DSA.<sup>[10]</sup> Fernandez *et al.* evaluated 38 patients with renal failure (25 men, 13 women, age range: 29-83 years) by captopril scintigraphy retrospectively for the presence of RAS. Of nine patients with a high probability, six had unilateral artery stenosis with subsequent improvement of BP and improvement or stabilization of GFR after revascularization (angioplasty: *n* = 3, bypass: *n* = 1) or appropriate medical treatment (*n* = 2) and one patient had unilateral thrombosis with contralateral artery stenosis. In the last patient, percutaneous angioplasty showed slow GFR deterioration. Two false-positive scans showed unilateral change after captopril and were of a patient with a predialysis diabetic nephropathy and another patient with left kidney atrophy and no RAS on arteriography. Ten patients (26%) were classified as having intermediate probability of RAS. Two had RAS that was confirmed in one by subsequent improvement in BP and GFR stabilization after angioplasty and visualized by magnetic resonance imaging in the second patient. In the other eight patients, RAS was ruled out on arteriography in four. Among four other patients, MRI showed no stenosis in one patient, two patients underwent ultrasonography that had negative results and the fourth patient had negative DSA results. Finally, in 19 patients with a low probability of RAS on captopril scintigraphy, five had no RAS on arteriography. A total of 40 patients probably did not have a renovascular pathology.<sup>[11]</sup>

Dubovsky *et al.*<sup>[12]</sup> in their study have reported percentage values of false-positive results of as high as 60%. False-positive results have also been found in many other conditions like glomerular disease (especially with vasculitic etiology, in nephrosclerosis, in conditions of sodium depletion.<sup>[13]</sup> Moreover there are several other conditions, which can mimic or be associated with an activation of the rennin-angiotensin-aldosterone axis such as hypotensive effects of ACEI, heart failure, state of

**Table 1: Probability of RAS by ACEI scan for small kidney**

	Total no.	CT/MR angiogram	
		Positive for RAS	Negative for RAS
High	10	4	6
Intermediate	12	0	12
Low	25	0	25

CT: Computed tomography; MR: Magnetic resonance; RAS: Renal artery stenosis; ACEI: Angiotensin converting enzyme inhibition

**Table 2: Comparison of <sup>99m</sup>Tc DTPA base and <sup>99m</sup>Tc DTPA ACEI scan patients with high probability for renovascular hypertension and comparison with CT/MR angiography**

Age/sex	Serum creatinine	BP	<sup>99m</sup> Tc DTPA renal scan				Change in GFR (%)	CT/MR angiography (RAS)
			Percentage of function		GFR (ml/min)			
			Baseline	Captopril	Baseline	Captopril		
47/female	1.7	170/100	31	19	20.6	10.8	-47.5	Positive
35/male	1.6	140/90	12	13	7.4	6.2	-16.2	Positive
55/male	1.6	140/94	19	11	12.1	4.9	-59.5	Positive
46/female	1.8	140/90	21	7	9.4	2.4	-74.4	Positive
23/male	0.8	110/70	19	17	23.7	15	-36.7	Negative
40/female	0.5	110/80	18	15	17	12.8	-24.7	Negative
60/female	0.6	140/80	45	45	40.3	34.8	-13.6	Negative
60/male	0.9	160/90	27	28	26.3	20.6	-21.6	Negative
51/female	0.7	140/90	31	25	24.7	17.9	-27.5	Negative
30/male	2.2	130/86	35	34	15.9	13.1	-17.6	Negative

CT: Computed tomography; MR: Magnetic resonance; RAS: Renal artery stenosis; DTPA: Diethylenetriaminepentacetic acid; ACEI: Angiotensin converting enzyme inhibition; GFR: Glomerular filtration rate; BP: Blood pressure

poor hydration and low urine flow, scleroderma, diabetic nephropathy, neurogenic bladder, and iatrogenic factors such as cyclosporine toxicity.<sup>[8]</sup>

## Conclusion

<sup>99m</sup>Tc DTPA ACEI renography is a safe, non-invasive, sensitive and cost-effective screening test for excluding renovascular hypertension in patients who have normal or nearly normal renal function in unilateral small kidney. It is simple to perform, widely available, relatively inexpensive, and consensus criteria for its interpretation exists. Only those patients of unilateral small kidney who are in the high probability group should be subjected to renal angiography for confirmation of RAS.

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**How to cite this article:** Hassan M, Khan SH, Ashraf M, Najar S, Shaheen F. <sup>99m</sup>Tc diethylenetriaminepentacetic acid angiotensin-converting enzyme inhibitor renography as screening test for renovascular hypertension in unilateral small kidney: A prospective study. *World J Nucl Med* 2014;13:159-62.

**Source of Support:** Nil