Angiotensin-converting Enzyme Inhibitor Radionuclide Renogram – A Non-invasive Tool to Suspect Renovascular Hypertension

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Abstract

Renal hypoperfusion due to renal artery stenosis (RAS) activates the renin–angiotensin–aldosterone system, leading to an elevated blood pressure (BP) that constitutes renovascular hypertension (RVH). Differentiation between RVH and RAS is essential because RAS is quiet in many non-hypertensive elderly persons. Furthermore, RAS is an associated but non-causative finding in a number of hypertensive patients. Angiotensin-converting enzyme inhibitors (ACEIs) renogram helps to detect RAS as the cause of hypertension and predicts curability or improvement in hypertension after intervention. ACEI renogram is most cost effective if used primarily in patients with moderate-to-high risk of RVH that includes abrupt or severe hypertension, hypertension resistant to three-drug therapy, bruits in the abdomen or flank, unexplained azotemia or recurrent pulmonary edema in an elderly hypertensive patient, or worsening renal function during therapy with ACEIs. In this report, we describe how ACEI renogram helped in the management of a patient with refractory hypertension due to RAS.

Key words: ACE inhibitor, renogram, DTPA, renal artery stenosis, renovascular hypertension

Introduction

A 42-year-old male who is a known smoker and alcoholic presented to the vascular surgery department with complaints of gripping pain in both lower limbs over the past 6 months. He is undergoing treatment for refractory hypertension (BP 200/130 mmHg) despite optimum medication comprising calcium channel blocker, beta-blocker, and diuretics over 6 years. His serum creatinine was 1.6 mg/dl while the blood sugar, electrolytes, cholesterol, and liver function tests were within normal limits. He is also being treated for chronic kidney disease (CKD) (estimated glomerular filtration rate [eGFR] = 27 ml/min/1.73m² at diagnosis) and possible bilateral renal artery stenosis (RAS) was considered. Contrast-enhanced computed tomography showed complete occlusion of the right renal artery with contracted right kidney and 70–80% occlusion at the origin of the left renal artery [Figure 1a and b]. Pan angiogram showed a significant peripheral vascular disease of both iliac arteries while the subclavian, carotid, and upper limb vessels were normal. He was treated for one episode of flash pulmonary edema 9 months ago. At that time, his echocardiography showed concentric LVH and global LVEF of 58%. There was no regional wall motion abnormality. ECG showed ST depression in II, III, and aVF, and therefore, he was started on statins also, along with aspirin. At the time of referral to our institution, his global LVEF was 43%.

We received him in our department to study the functional significance of RAS with 99mTechnetium-DTPA renogram with angiotensin-converting enzyme inhibitors (ACEIs). The patient was prepared as per the Society of Nuclear Medicine and Molecular Imaging guidelines for baseline and ACEI renogram (2 days protocol).[1] He was allowed to continue his medication during the study period. On day 1, baseline renogram was performed by giving intravenous injection of 100 MBq of 99mTc-DTPA in 1.0 ml saline through an intravenous cannula. Sequential dynamic and periodic static images of the abdomen

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were acquired in posterior view (patient in supine position) using a dual-headed gamma camera (GE-Discovery NM 670, USA). Similar study was repeated the next day 1 h after oral administration of 10 mg Enalapril. Blood pressure (BP) in the right upper limb was continuously monitored with the patient in supine position and was found to maintain around 200/130 mmHg. There was no change in BP 1 h after enalapril administration.

The left kidney showed adequate cortical function with timely tracer transit into pelvis and unobstructed subrenal drainage at baseline study. During ACE inhibition (ACEI), it showed marked parenchymal retention and prolonged intraparenchymal tracer transit, suggesting a high probability of renovascular hypertension (RVH) [Figure 2a and b]. The right kidney did not show any tracer uptake, suggesting non-functional status. The left kidney renogram showed an upsloping pattern of time activity curve during ACEI [Figure 3a and b]. Six different patterns of renogram curves have been described in literature, based on the renal excretory function. They are as follows: 0 normal; 1 minor abnormalities, but with T\text{max} > 5 min and a 20-min/max cortical ratio > 0.3; 2 a marked delay in excretion rate with preserved washout phase; 3 delayed excretion rate without washout phase (accumulation curve); 4 renal failure pattern with measurable kidney uptake; and 5 renal failure pattern without measurable kidney uptake. Our patient’s baseline renogram showed Type 1 curve which changed to Type 3 during ACEI which represents a high probability for RVH. Quantitative estimates also confirmed the impairment in renal function and prolongation of tracer transit time after ACEI by demonstrating >10% reduction in GFR and >0.15 increase in the 30-min/peak

Figure 1: Coronal section of contrast-enhanced computed tomography KUB showing smaller right kidney (a). Digital subtraction angiogram showing narrowing at the origin of the left renal artery with post-stenotic dilatation and complete occlusion with non-visualization of the right renal artery (b)

Figure 2: 2 min/frame images of renogram at baseline (a) and during angiotensin-converting enzyme inhibitors (ACEIs) (b). The left kidney shows adequate tracer uptake followed by timely transit into pelvis and excretion into the bladder by 8th min (a). After ACEI, there is a continuous accumulation of tracer in the left kidney with delayed transit into the pelvis and delayed excretion into the bladder by 16th min. An increase in background activity is also seen suggesting impaired tracer clearance by the left kidney. After ACEI, significant tracer retention can be noted in the left kidney at the end of dynamic study (the last frame corresponding to 30th min) compared to baseline study.
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The Society for Cardiovascular Angiography and Interventions has issued Expert Consensus Statement on the appropriateness criteria for Renal Artery Stenting.[5] Our patient’s clinical presentation of flash pulmonary edema, resistant hypertension, and CKD with eGFR <45 cc/min with bilateral significant RAS meets the appropriateness criteria for revascularization of his left RAS.[5] Demonstration of the hemodynamic significance in moderate RAS (50%–70%) by invasive angiography (IA) with measures such as fractional flow reserve and translesional gradient is required before planning stenting. IA has its own potential complications like contrast-induced nephropathy in patients with ischemic nephropathy and procedure-related complications such as pseudoaneurysm and hematoma. ACEI renogram could be considered as a safe non-invasive procedure that can demonstrate the contribution of RAAS to hypertension and the potential complications with IA can be avoided. IA could be averted with negative ACEI renogram, while a therapeutic IA can be planned following a positive ACEI renogram.

Conclusion

a) In our patient with CKD due to bilateral RAS, ACEI renogram diagnosed RVH due to the left RAS and confers a high probability of recovery following successful revascularization.
b) In young patients with refractory hypertension, ACEI renogram could be considered as one of the first-line investigations to identify a potentially curable cause of secondary hypertension, i.e., RAS.
c) ACEI renogram can be safely performed in CKD patients since it uses only micromolar quantity of

<table>
<thead>
<tr>
<th>Renogram parameters</th>
<th>Left kidney</th>
<th>Baseline</th>
<th>ACEI</th>
</tr>
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<tbody>
<tr>
<td>Time to peak, Tmax (min)</td>
<td>5.92</td>
<td>13.44</td>
<td></td>
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<tr>
<td>Peak to ½ peak</td>
<td>12.75</td>
<td>91.15</td>
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<tr>
<td>30 min/peak ratio</td>
<td>0.43</td>
<td>0.87</td>
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<tr>
<td>30 min/3 min ratio</td>
<td>0.55</td>
<td>1.53</td>
<td></td>
</tr>
<tr>
<td>GFR (ml/min/1.73 m²)</td>
<td>50.31</td>
<td>31.01</td>
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ACEI: Angiotensin-converting enzyme inhibitors, GFR: Glomerular filtration rate

ratio and 3 min increase in the $T_{\text{max}}$ from the baseline study, respectively [Table 1].

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b) In young patients with refractory hypertension, ACEI renogram could be considered as one of the first-line investigations to identify a potentially curable cause of secondary hypertension, i.e., RAS.
c) ACEI renogram can be safely performed in CKD patients since it uses only micromolar quantity of
radiopharmaceutical (i.e., 99mTc-DTPA) that causes no functional overload to the kidneys unlike angiogram, which carries a risk of contrast-induced nephropathy/nephrogenic systemic fibrosis.

d) DTPA renogram can be used to assess the differential renal function in patients with bilateral significant RAS to guide optimal therapeutic strategy.

References


