Renal Scintigraphy with Angiotensin-Converting-Enzyme (ACE) Inhibition

**Primary Indications:** Diagnosis of renovascular hypertension.

**Rationale:** Hemodynamically significant renal arterial stenosis causes decreased renal arterial perfusion pressure, resulting in a decrease in glomerular filtration pressure and glomerular filtration rate (GFR). As a compensatory mechanism, the affected kidney secretes renin. Renin cleaves angiotensinogen to form angiotensin I, which in turn is cleaved by angiotensin-converting enzyme (ACE) to angiotensin II. Angiotensin II leads to hypertension both because it is a potent systemic vasoconstrictor and because it stimulates the secretion of aldosterone by the adrenal glands. Additionally, a local intrarenal effect of angiotensin II is efferent glomerular arteriolar vasoconstriction, thereby preserving glomerular filtration pressure and the GFR. Angiotensin-converting-enzyme (ACE) inhibitors prevent the conversion of angiotensin I to angiotensin II, thereby reversing the vasoconstriction in the efferent arterioles. The resultant decrease in glomerular filtration pressure in a kidney with hemodynamically significant renal arterial stenosis can result in a dramatic decrease in GFR and in the urine flow rate in the renal tubules. Renal blood flow can actually increase (because of a reduction in the overall resistance in the renal vascular bed).

Recently, a new class of class of drugs (angiotensin II-receptor antagonists) have been introduced. Losartan (Cozaar) is the first member of this class to receive FDA approval. Although these drugs interfere with the renin-angiotensin system via a different mechanism than ACE inhibition, the effects on renal function are similar.

ACE-inhibited renal scintigraphy can be used to demonstrate the reversible pathophysiology associated with renovascular hypertension. Finding reversible renal dysfunction predicts the likelihood that a patient’s hypertension will respond to a revascularization procedure. Renal artery stenosis and renovascular hypertension are not synonymous.

In general, it is sufficient to perform only a single-stage ACE-inhibited study in patients with normal renal function. A two-stage study, consisting of both baseline and ACE-inhibited renal scintigraphy, is recommended in patients with impaired renal function (serum creatinine > 2.0 mg/dL) and in patients in whom performing a subsequent baseline study, if required, on another day would be impractical (e.g., because the patient lives a long distance from the hospital).

**Interfering Conditions:** The reliability of the test is reduced in patients with moderate to severe impairment of renal function.

Chronic diuretic therapy increases the risk of marked hypotension when the ACE inhibitor is administered; thus, diuretics generally should be discontinued 1-3 days before the test.

Chronic ACE inhibitor therapy generally should be discontinued before the test. If discontinuation of ACE inhibitor therapy is impractical, per-forming conventional renal scintigraphy while the patient is maintained on the medication may provide equivalent information to that from ACE-inhibited renal scintigraphy. Treatment with ACE inhibitors should be stopped for the following minimum periods of time before the test:

- **1 day:** Captopril (Capoten, Capozide)
- **3 days:** Other ACE inhibitors [Benazepril (Lotensin); Enalapril and Enalaprilat (Vasotec, Vaseretic); Fosinopril (Monopril); Lisinopril (Zestril); Quinapril (Accupril); Ramipril (Altace)]

Angiotensin II-Receptor Antagonists [Losartan (Cozaar)]
Precautions: Hypotension is a side effect of ACE inhibitors. To minimize the risk of marked hypotension, the following precautions should be observed.

- Baseline diastolic pressure should be greater than 80 mm Hg.
- Baseline systolic pressure should be greater than 120 mm Hg.
- Hydrate patient both orally and intravenously.
- Obtain and record blood pressure and pulse every 10 minutes.

Angioedema is a side effect of ACE inhibitors, and resultant laryngeal edema can be fatal. If angioedema develops during injection of enalaprilat, the injection should be discontinued immediately. The patient should receive prompt treatment with 0.3-0.5 ml of 1:000 epinephrine subcutaneously if there is any sign of airway obstruction.

Radiopharmaceutical: Tc-99m Mertiatide (Tc-99m MAG3)

Adult Dosage: 7.5 mCi, if only ACE-inhibited renal scintigraphy to be performed.
1.0 mCi and 9.0 mCi for baseline and ACE-inhibited renal scintigraphy, respectively, if both are to be performed on the same day.

Pediatric Dosage: 100 μCi/kg with a minimum dosage of 1.0 mCi, if only ACE-inhibited renal scintigraphy to be performed.
15 μCi/kg (with a minimum dosage of 150 μCi) and 120 μCi/kg (with a minimum dosage of 1.2 mCi) for baseline and ACE-inhibited renal scintigraphy, respectively, if both are to be performed on the same day.

Radiation Dosimetry: Adult (7.5-mCi dosage). Critical organ (bladder wall): 3.05 rem. Effective dose: 0.20 rem.
Infant (1-year; 100 μCi/kg dose). Critical organ (bladder wall): 1.18 rem. Effective dose: 0.08 rem.
(Dosimetry is altered in the setting of impaired renal function. For example, in renal failure, gastrointestinal tract doses are increased, although effective dose is slightly decreased. With acute unilateral obstruction, the dose to the obstructed kidney is substantially increased.)

Route of Administration: Intravenous

Pharmacologic Drug: Enalaprilat (Vasotec for intravenous use) or Captopril (for oral use)

Enalaprilat Dosage: 0.04 mg/kg; maximum total dose - 2.5 mg

Enalaprilat Route: Intravenous; dose should be diluted in 50 mL normal saline solution and injected over 5 minutes.

Captopril Adult Dosage: 50 mg tablet – crushed and dissolved in 150 mL water

Captopril Route: Orally.

Patient Preparation: ACE inhibitors and diuretics should be discontinued before the study (see Interfering Conditions).
The patient should be well hydrated for the examination (see Precautions and Procedure).

**Equipment Setup:** Gamma Camera: LFOV camera for studies in adults with zoom; SFOV or zoomed LFOV camera for studies in small children. Collimator: LEAP for studies in adults. For studies on the portable camera, a diverging collimator should be used for adults and a LEAP or converging collimator for small children or infants. Gamma camera detector below imaging table to allow for posterior imaging for conventional studies; see below.

Energy Window: 140 keV with 20% window

**Patient Positioning:** Supine (with camera beneath table for posterior imaging)

**Procedure:** ACE-Inhibited Renal Scintigraphy Only
The patient should be well hydrated for the examination. Unless otherwise specified by the physician, the patient is to be hydrated prior to starting the study with approximately 16 ounces (500 mL) of water orally (for a 70-kg adult). If this is not possible, the patient should be hydrated using intravenous fluids. Adults should be hydrated with 500 mL of normal saline infused intravenously over 30 minutes starting 15 minutes prior to radiopharmaceutical administration. For children weighing more than 35 kg, 500 mL 5% dextrose/0.5 normal saline solution should be infused over 30 minutes starting (approximately 5 drops per second) 15 minutes prior to radiopharmaceutical administration. Smaller children should receive appropriate hydration based on body weight, using 5% dextrose/0.5 normal saline solution at a dose of 0.5 mL/kg/min (maximum 500 mL) infused over 30 minutes starting 15 minutes prior to radiopharmaceutical administration.

Baseline blood pressure and pulse should be measured and recorded with the patient in the standing and supine positions. Baseline diastolic pressure should be greater than 80 mm Hg. Baseline systolic pressure should be greater than 120 mm Hg. Blood pressures and pulses should be measured and recorded every 10 minutes thereafter until the completion of the procedure. The actual times (24-hr clock) for the vital signs, infusions and imaging should be written on the patient data sheet by the technologist performing the study.

A secure intravenous line should be established, and a continuous intra-venous infusion of normal saline solution at the rate of 10 mL/min (approximately 200 drops per minute) should be initiated. (For pediatric patients, scale administered fluid volume based on body weight—0.15/mL/kg/min.) After 5 minutes of saline infusion, begin the intravenous injection of enalaprilat. The weight of the patient in kilograms and the amount of the drug in milligrams must be recorded on the patient data sheet. The drug is to be given diluted in 50 mL normal saline solution over a period of 5 minutes (see Time-line diagram). The nuclear medicine physician will be present during the pharmacological infusion. The continuous infusion of normal saline solution should be resumed after completing the enalaprilat injection. Ten minutes later show the nuclear medicine physician the pulse and blood pressure data so they can determine if the patient had the appropriate patient response before administering the radiopharmaceutical. Fifteen minutes later, the radiopharmaceutical should be injected, and acquisition of conventional renal images should be started (see Renal Scintigraphy procedure). Continuous renal imaging should be performed for 20 minutes after radiopharmaceutical injection.

IV normal saline infusion (10 mL/min)MinutesMeasure and record BP and pulse every 10 min0102030405-min IV enalaprilat injectionInject radiopharmaceutical 15 min after enalaprilat injectionRoutine renal scintigraphy50
At the end of the study the patient’s supine pulse and blood pressure should be measured and recorded, the patient should sit on the stretcher, and the blood pressure and pulse should again be measured and recorded. If the patient remains asymptomatic, the patient should stand, and the blood pressure and pulse should be measured and recorded. If the patient is symptomatic or if either the sitting or standing blood pressure is 10 mm Hg less than baseline, consult physician.

The patient data sheet and the images should be provided to physician for review. With physician approval, the intravenous line can be removed and the patient allowed to leave.

Baseline and ACE-Inhibited Renal Scintigraphy
If baseline renal scintigraphy is to be performed, the procedure is modified as follows.
As above, the patient should be hydrated orally, a secure intravenous line placed, and intravenous infusion of normal saline solution begun at a rate of 2 mL/min (40 drops/min) (with appropriate scaling in children based on body weight—0.03/mL/kg/min). Baseline blood pressure and pulse should be measured and recorded with the patient in the standing and supine positions. The first dosage of (1.0 mCi) radiopharmaceutical should be injected, and acquisition of conventional renal images should be started (see Renal Scintigraphy procedure). Continuous renal imaging should be performed for 20 minutes after radiopharmaceutical injection. A post-void image should also be acquired according to the standard Renal Scintigraphy procedure.

After completion of the post-void image, the rate of infusion of normal saline solution should be increased to 10 mL/min and the patient's blood pressure and pulse should be measured and recorded in the supine, sitting, and standing position. Injection of enalaprilat and renal scintigraphy with the second dosage of radiopharmaceutical should be performed as described above. Assessment of the patient's condition also should be performed as described above.

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<tr>
<th>View</th>
<th>Analog (if available)</th>
<th>Digital</th>
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<td>Standard renal acquisition (applies to ACE-inhibited and/or baseline studies)</td>
<td>See Renal Scintigraphy protocol</td>
<td>See Renal Scintigraphy protocol</td>
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**Items Required For Complete Study:**

1. **Radionuclide angiogram and sequential images:** Film using Display, Renal Flow and Renal Function. If not using the preset formatting, a —D‖ display (Discrete image-by-image scaling) should be used for the radionuclide angiogram and a —U‖ display (Uniform scaling) should be used for the sequential images.

2. **Post-void image:** routinely obtained with baseline study if this is performed on the same day as ACE-inhibited renal scintigraphy.

3. **Transfer of all digital images to work station:** processing will be performed by a physician.