

## The choice of radiopharmaceuticals and imaging procedures in patients with hydronephrosis and suspected renovascular hypertension

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Dynamic renal scintigraphy is carried out by radiopharmaceuticals which are eliminated via kidneys. It provides information about renal parenchymal function and drainage. Modifications of the standard dynamic renal scintigraphy used for specific indications are diuresis renography and angiotensin-converting enzyme inhibitors (ACEIs) renography. Radiopharmaceuticals used for these methods are listed in table 1. Tracers extracted from the blood stream by renal tubules have a greater initial renal uptake than  $^{99m}\text{Tc}$ -DTPA resulting in a higher kidney to background ratio. For these reasons, the tubular agents are preferred to  $^{99m}\text{Tc}$ -DTPA for diuretic renography, especially in infants because their kidneys are immature and have physiologically slow renal clearance up to two years of age ensuing in low renal uptake of tracer with a high background activity. Because of its higher extraction,  $^{99m}\text{Tc}$ -MAG3 is preferred over  $^{99m}\text{Tc}$ -DTPA in patients with renal insufficiency even when the affected kidney's split function is less than 25% for ACEI renography, although DTPA may be more efficacious in patients with segmental renal artery stenosis (RAS).

Table 1. Radiopharmaceuticals for diuretic and ACEI renography

Radiopharmaceuticals	Kidney pathway
$^{99m}\text{Tc}$ -diethylene triamine pentaacetic acid ( $^{99m}\text{Tc}$ -DTPA)	Glomerular filtration
$^{123/131}\text{I}$ -orthoiodohippurate (OIH, Hippuran)	Tubular extraction and secretion (80%) Glomerular filtration (20%)
$^{99m}\text{Tc}$ -mercaptoacetyltriglycine ( $^{99m}\text{Tc}$ -MAG3)	Tubular extraction and secretion
$^{99m}\text{Tc}$ -Ethylenedicysteine ( $^{99m}\text{Tc}$ -EC)	Tubular extraction and secretion

Diuresis renal scintigraphy is a useful method in the investigation of hydronephrosis (dilatation of the pelvicalyceal system) and hydroureteronephrosis (dilatation of the pelvicalyceal system and ureter) capable to differentiate between a true obstruction and a dilated nonobstructed system (stasis) after the intravenous injection of furosemide (Lasix). Distension of the collecting system and ureter may be caused by an obstructed renal pelvis or ureter, vesicoureteral reflux, infection, posterior urethral valves or a full bladder as well. Other imaging techniques, such as contrast intravenous urography, ultrasonography and standard radionuclide renography, cannot reliably differentiate renal stasis caused by obstruction from nonobstructive pattern. On the other hand, Whitaker's test, established as a gold standard for diagnosis of renal obstruction, is rather invasive.

Diuresis renography is based on diuretic effect of furosemide (Lasix) on kidney. Furosemide acts on the loop of Henlé, a structure of the kidney involved in reabsorbing water. It encourages kidneys to remove more water from the blood and pass it into the urine, producing more urine. In the presence of obstruction, the increased urine flow failed to overcome the obstacle in the collecting system or ureter and tracer elimination from kidney does not occur. The diuretic effect usually begins within 1-2 min and reaches the maximal effect 15-18 min after intravenous injection of the furosemide. The dose of Lasix for diuresis renography is 1.0 mg/kg with the usual maximum dose of 40 mg in adults and of 20 mg in children. Higher diuretic dose may be required in patients with severe renal failure.

Oct. 14

Abstracts

Depending on the time of furosemide application, three protocols for diuresis renography are adopted. Diuretic can be injected 20 min after the radiopharmaceutical application (F+20 protocol), 15 min prior to the radiopharmaceutical application (F-15) or simultaneously with radiopharmaceutical (F-0). The choice depends on supposed pathological condition and the age of a patient. In F+20, the most commonly used protocol, furosemide is injected at the time when the renal pelvis and ureter occur maximally distended in hydronephrosis and hydroureter. Acquisition time is about 40 min (20 min prior to and 15-20 min after diuretic application). When the patient has enormous dilated pelvicalyceal system as previously seen on ultrasonography, F-15 protocol is the best choice. Using this protocol, imaging is performed for 20 min after the injection of the radiopharmaceutical. This approach is also recommended when F+20 results are equivocal or the renography under a state of maximal diuresis is required (1, 2). F-0 protocol (1) is the most popular since it is less invasive and requires shorter imaging time compared with F+20 study. It is of a great importance in young children as the establishing of venous access in them is often difficult since the veins are small and subcutaneous fat may be prominent. In addition, some young children cannot lie down still for 40 min necessary for F+20 renogram. This method offers sufficient sensitivity, specificity and accuracy in differentiating obstruction pattern and was shown more sensitive in children with pelviureteric junction and vesicoureteric junction obstruction relating to children in whom obstruction was caused by other urinary tract diseases (3). Furthermore, this protocol allows clarification in cases of equivocal F+20 studies (2). The post micturition (PM) one minute images within 60 min after the radiopharmaceutical administration are recommended as a part of each protocol mentioned above to enable the analysis of kidneys when bladder is empty. In the presence of a full bladder, drainage from kidney may be postponed ensuing in a flat renal curve, even in normal kidney. The PM images are performed in supine position of a patient, after at least 5 min upright position and voiding. That permits gravity to act and to decrease obvious poor renal drainage due to the supine position.

Interpretation of the response to the diuretic includes visual analysis of renal frames associated with analysis of shape of the post-diuretic curve obtained from region of interest around whole kidney or collecting system. Apart from this, quantitative parameters, such as residual activity after the PM images (a percentage of the peak of the renogram) and furosemide clearance half-time ( $T_{1/2}$ , the time at which the time-activity curve falls to half of its maximal activity) are analysed. The obtained results are reported as obstruction when the increase of the activity proximal to obstruction, ascending curve and  $T_{1/2} > 20$  min are found. On the other hand, absence of obstruction is characterized by rapid and almost complete tracer washout, normal post-diuretic curve and  $T_{1/2} < 10$  min, although the definitive exclusion of obstruction may still require an invasive study. Equivocal finding is defined as partial tracer emptying, delayed down-slope of the curve and  $T_{1/2}$  between 10 and 20 min.

ACEIs renal scintigraphy is a very sensitive and specific non-invasive procedure for the diagnosis of reno-vascular hypertension caused by renal artery stenosis in selected hypertensive population and prediction of the revascularisation outcome with respect to blood pressure response (4, 5). Another approach, such as scintigraphy with angiotensin II receptor antagonists was proven to be less sensitive than captopril renography (5). Although intra-arterial digital subtraction angiography is still considered the standard of reference test for the anatomical diagnosis of RAS, noninvasive techniques apart from ACEI renography, such as MRI angiography (especially in patients who are likely to have stenosis located in the proximal third of the renal artery), CT angiography, and duplex sonography also allow visualization of functional RAS.

ACEI renography is based on comparison of renograms of an adequately hydrated patient before and after ACE inhibition. Maintenance of the glomerular filtration rate in patients with haemodynamically significant RAS depends on increased efferent glomerular arteriolar tone mediated by angiotensin II. In the kidney with a functional RAS, ACEIs preventing conversion of angiotensin I to angiotensin II, decrease the glomerular filtration rate by suppressing the angiotensin II mediated efferent arteriolar vasoconstriction, and thus decrease the intratubular urine flow in the kidney (4). Captopril or enalaprilat are the most commonly used for ACEI scintigraphy. Captopril is given orally 25-50 mg, 60 min before radiopharmaceutical administration since peak blood levels occur at that time. Enalaprilat is administered intravenously over 3-5 min in a dose of 0.04 mg/kg (maximum 2.5 mg), 10-15 min prior to the radiopharmaceutical administration. Thus, the procedure is shorter than that with captopril, and potential problems with gastrointestinal absorption are avoided.

Oct. 14

Abstracts

The choice of protocol may depend on the expected finding of the test according to patient's history, clinical clues and previous examinations. Namely, if there is a relatively low probability for reno-vascular hypertension, 2 days protocol is better because baseline study on the second day is not needed in the case of normal post-captopril renogram. In patients with expected high probability of RAS, one or two day protocol may be advocated, stressing that the former requires that the patient stays in department for a longer period of time, yet the whole study is finished in one day.

Interpretation of the test is based on the analysis of whole-kidney or renal parenchyma curves. The latter is advocated if there is retention of activity in pelvis or calyces. In kidneys affected with haemodynamically significant RAS, post-ACEI renogram is characterized by reduction in relative kidney uptake, prolongation of the parenchymal transit time, an increase in residual activity, and prolongation of the time to maximum activity. When tubularly secreted radiopharmaceuticals are employed, unilateral parenchymal retention after ACEI is the most important criterion for reno-vascular hypertension.

Conclusion: The choice of imaging protocols and radiopharmaceuticals in patients with hydronephrosis and suspected renal artery stenosis may depend on several factors, such as possible findings of the procedure according to patient's history, clinical signs and previous examinations, the age of patient and renal function.

#### References

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