The value of scintigraphy in diagnosis of renal disease

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Renal imaging with radioisotopes, or renal scintigraphy, allows the quantitative evaluation of renal function and urodynamics. Measurement of renal function provides essential information in various situations of clinical practice. Angiotensin-converting enzyme inhibitor renography makes it possible to detect patients with renovascular hypertension. Diuresis renography aids in differentiating urinary obstruction from unobstructed dilatation. Renal scintigraphy is a valuable tool in the observation of grafts after renal transplantation. In this review, the basic aspects and major clinical applications of renal scintigraphy are discussed.

Introduction

Nuclear imaging with radioisotopes provides functional information, whereas other imaging procedures such as radiography, ultrasonography, computed tomography, and magnetic resonance imaging yield mainly morphological information. Although renal scintigraphy, or radionuclide renography, is relatively weak in depicting anatomical abnormalities and space-occupying lesions, it permits sensitive, noninvasive, quantitative assessment of renal function and urodynamics. Renal scintigraphy is a valuable tool to determine appropriate patient management in the clinical practice of nephrourology. It is also beneficial that radiotracers for renal scintigraphy have essentially no nephrotoxicity, unlike x-ray contrast materials.

Radiotracers-radiopharmaceuticals

In nuclear imaging tests, a radioactive tracer is administered to the patient, and gamma rays emitted from the patient are externally detected with a gamma camera, to produce images that reflect the distribution of the radiotracer. The information obtained from these examinations depends mainly on the phamacokinetics of the radiotracer used. Radiotracers for dynamic renal scintigraphy include ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA), ^{99m}Tc-mercaptoacetyl triglycine (MAG3), and ^{99m}Tc dimercaptosuccinic acid (DMSA). These tracers are rapidly taken up by the kidney and then excreted into the urinary tract. Serial frames of the posterior view are acquired for 20-30 minutes immediately after tracer injection. The frame rate is 1-3 seconds per frame for about one minute to assess perfusion (perfusion phase), 10-15 seconds per frame for about four minutes to assess function (function phase), and then 10-30 seconds per frame to assess the urinary system (excretion phase).

The mechanism of renal uptake and imaging characteristics differ among the dynamic renal agents. DTPA is taken up by the kidney through glomerular filtration and is not secreted or reabsorbed by the renal

tubules. Once it reaches the kidney, about 20% is accumulated and the remainder flows away. That is, the extraction fraction of DTPA is 20%, a value approximating the filtration fraction. MAG3 is taken up by the proximal renal tubules. It shows high plasma protein binding and cannot be filtered through the glomerular membrane. Its high extraction fraction of approximately 50% makes it possible to acquire high-quality images. Although its extraction fraction is approximately 80%, problems linked to the physical characteristics of radioactive iodine interfere with the acquisition of high-quality images, especially during the perfusion phase. Renal scintigraphy with DTPA provides glomerular filtration rate (GFR) as a quantitative measure of renal function The index of renal function obtained using MAG3, termed tubular excretion rate or MAG3 clearance, does not correspond to a well-known parameter; however, it is closely correlated with, and can be converted to ERPF. [1]

^{99m}Tc-dimercaptosuccinic acid (DMSA) remains in the renal parenchyma for an extended period and is utilized for static renal scintigraphy. It accumulates in the functioning renal cortex, and impaired renal cortex and space occupying lesions are depicted as hypoactive areas. Static renal scintigraphy with DMSA is established for the diagnosis of acute pyelonephritis and detection of renal scars. [2]. In the following sections, dynamic renal scintigraphy, a comprehensive method of evaluating nephro-urological function, is discussed.

Interpretation

In visually interpreting dynamic renal scintigrams, delineation of the renal parenchyma and urinary tract are assessed as functions of time. Parenchymal visualization during the perfusion phase principally depends on delivery of the tracer through the vascular system. Visualization during the following period is determined by the plasma concentration of radiotracer, renal clearance, and renal parenchymal transit time. The tracer accumulates in the parenchyma at a rate corresponding to plasma concentration multiplied by renal clearance, is retained during transit time, and then is excreted into the urinary system. During the function phase, because most of the tracer trapped by the kidney is retained and plasma concentration remains almost unchanged, visualization of the renal parenchyma is determined almost exclusively by renal clearance, reflecting GFR for DTPA and tubular function for MAG3. High renal function yields strong visualization, and low function weak visualization. In unilateral hypofunction, decreased accumulation is shown in the diseased kidney. Focal hypoactive areas may be seen at sites of focal renal damage caused by pyelonephritis, renal infarction, and so on.

The tracer begins to escape the renal parenchyma 3-4 minutes after injection and appears in the collecting system. Determination of parenchymal delineation is more complex during the excretion phase than during the function phase. High renal function causes a rapid reduction in the plasma concentration of tracer, resulting in rapid weakening of the visualization. Plasma concentration remains relatively high in patients with low function, and the weakening of parenchymal visualization with time is less apparent. On the other hand, prolongation of renal parenchymal transit time leads to prolonged retention, and washout from the parenchyma is delayed. The transit time is prolonged in various conditions including urinary obstruction, renal artery stenosis, and acute tubular necrosis. A progressive increase in parenchymal activity is a typical finding of acute tubular necrosis in renal scintigraphy with MAG3. Dehydration and distended bladder may prolong parenchymal transit time, owing to slow urine flow, in the absence of renal disorders, and sufficient hydration and voiding is required as patient preparation, to avoid non-pathological prolongation of transit time. Tracer washed out of the renal parenchyma flows from the collecting system into the bladder. Rapid transfer to the bladder suggests normal passage through the urinary tract. Retention in the upper urinary tract may be a result of urinary obstruction or simple dilatation without obstruction. Differentiation between them is clinically essential, but difficult, and often requires diuresis renography.

Quantitative evaluation plays a critical role in interpreting dynamic renal scintigraphy. Although renal function can be roughly assessed by visual inspection of initial renal uptake, quantitative analysis provides an objective, detailed evaluation. Angiotensin converting enzyme inhibitor (ACEI) renography is performed for the diagnosis of renovascular hypertension, and diuresis renography for urinary obstruction. Interpretations of these examinations rely on computer-generated renograms and quantitative indices calculated from the renograms.

Camera-based methods, which depend on the fact

that renal uptake early after tracer injection reflects renal function, can calculate renal function from imaging data alone without blood sampling. [5], [6] First, a region of interest (ROI) is drawn for each kidney to estimate activity in the renal area The background-subtracted, attenuation-corrected renal activity is normalized to the injection dose, and is substituted in an empiric equation to obtain renal clearance; total renal function is measured by the former and divided into right and left functions based on the imaging data. Attention should be paid to technical problems in evaluating renal function by camera-based methods. Renogram curves offer an overview of the time course of renal radioactivity and can be generated by setting an ROI for each kidney. Radioactivity in a kidney ROI derives from the renal parenchyma, upper urinary tract, and overlapping extrarenal tissues. After successful background subtraction, a renogram can reflect the temporal profile of the sum of radioactivities in the renal parenchyma and upper urinary tract. A renogram in a normal subject (Fig. 1), demonstrates rapid increase during the perfusion and function phases, followed by rapid decline during the excretion phase. Hypofunction flattens the slopes during both the function and excretion phases. Urinary obstruction causes delayed excretion; however, a renogram cannot discriminate between retention in the renal parenchyma and that in the urinary tract, and visual assessment of scintigraphic images is required.

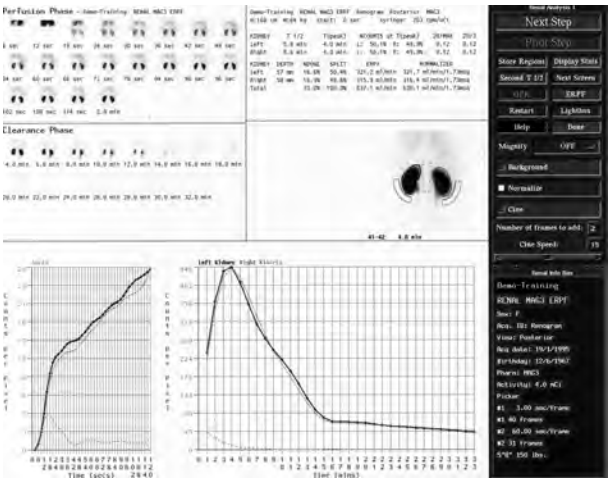


Fig. 1: Normal renogram

Clinical Applications

Estimation of Split Renal Function

Renal scintigraphy permits quantitative, noninvasive, rapid measurement of GFR or ERPF and can detect decline in renal function at an early stage.

Estimation of split renal function is a particularly important role of renal scintigraphy. The estimation of split renal function is essential when asymmetric renal hypofunction may be present or surgical intervention is under consideration.

Asymmetric renal hypofunction may occur in various conditions such as congenital abnormalities, pyelonephritis, vesicoureteral reflux, obstructive nephropathy, vascular disorders, space-occupying lesions, and post-traumatic changes. Unilateral hypofunction in patients with vesicoureteral reflux or urinary obstruction suggests that the abnormality in the urinary tract injures the renal parenchyma and that early surgical intervention may aid in preserving renal function. Renal function of the involved side may be decreased in patients with renal malignancy, and the estimation of split renal function contributes to predicting postoperative function. When the necessity of dialysis after radical nephrectomy is predicted because of contralateral hypofunction, nephron-sparing surgery may be selected. Although the significance of the technique resides in its ability to preserve renal function as much as possible. Estimation of split function aids in assessing preserved function postoperatively as well as in determining the indication for the technique preoperatively. Live kidney donors often show asymmetric function, and renal scintigraphy contributes to determining the side of harvest. [10]

Renovascular hypertension

Diagnosis of renovascular hypertension is an important role of renal scintigraphy. Renovascular hypertension is caused by renal hypoperfusion resulting from renal artery stenosis and consequent activation of the renin-angiotensin system. It should be noted that renal artery stenosis is common in hypertensive patients but is not necessarily the cause of hypertension. The aim of ACEI renography is not to detect patients with anatomical stenosis of the renal artery but to detect those who have hemodynamically significant renal artery stenosis as the cause of hypertension.

The reduction of renal perfusion pressure by renal artery stenosis stimulates the secretion of renin. Renin converts angiotensinogen to angiotensin I, which is converted to angiotensin II by angiotensin-converting enzyme. Angiotensin II constricts efferent arterioles of the affected kidney, leading to a rise in the pressure gradient across the glomerular capillary membrane. As

a result, glomerular filtration of the affected kidney is maintained despite hypoperfusion. ACEI disturbs the compensatory mechanism and diminishes GFR and urine flow. Renal scintigraphies at baseline and one hour after oral intake of captopril are compared for the diagnosis of renovascular hypertension. Findings indicative of renovascular hypertension include worsening of the renogram curve and a decrease in split function after ACEI administration. Decrease in split function is chiefly observed for DTPA and less frequently for MAG3. Renograms are classified, from better to worse, into normal, mildly delayed, moderately delayed, severely delayed or obstructive, hypofunctional, and non-functional. Worsening of a renogram is attributable to decrease in split function and parenchymal retention owing to reduced urine flow. It is mainly judged by visual interpretation of the curve, and renogram parameters [ratio of counts at 20 minutes after injection to peak counts (T20/Tmax) or time to maximum counts (Tmax)] may be used as complements.

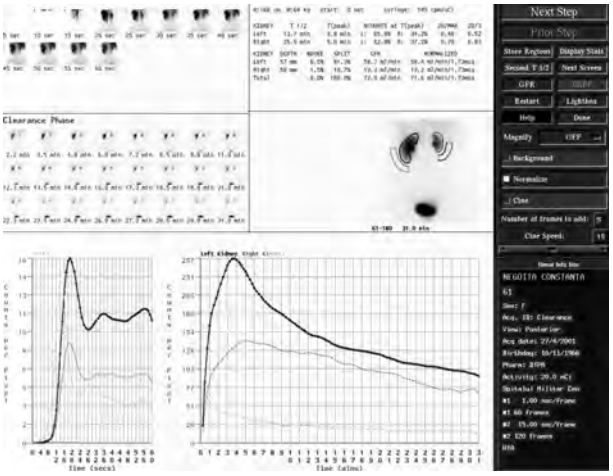


Fig. 2: Split function in renogram with ACEI

ACEI renography provides clinically essential information. Sensitivity and specificity have been reported to be 80-100% for the diagnosis of renal artery stenosis in patients clinically suspected of having renovascular hypertension. More importantly, positive ACEI renography indicates a high probability, exceeding 90%, of blood pressure reduction after revascularization. [12]

Urinary obstruction

Dilatation of the upper urinary tract may indicate urinary obstruction; however, nonobstructive, simple dilatation is frequent. Obstruction may result in progressive renal parenchymal damage, while simple dilatation does not cause clinically significant problems. Distinction between the two conditions is critical for deciding appropriate patient management. The distinction cannot be made by morphological imaging methods, such as drip infusion pyelography, ultrasonography, or computed tomography. Diuresis renography provides information on urodynamics as well as renal function, and its usefulness has been accepted for the evaluation of urinary obstruction.

In diuresis renography, furosemide is administered intravenously, and washout of the tracer from the kidney and collecting system is evaluated at the induced high rate of urine flow. [13],[14] Furosemide is commonly administered 20 minutes after tracer injection (F+20 study) to allow the tracer to accumulate in the collecting system. When the result of the F+20 study is equivocal, furosemide injection at 15 minutes before tracer injection (F-15 study) may be helpful. In both obstruction and simple dilatation, renography without the injection of furosemide may show retention of the tracer in the kidney and collecting system. The administration of furosemide accelerates washout in simple dilation. In contrast, washout is prevented in obstruction, and tracer remains even at the high urinary flow rate. Differentiation can be made by visual interpretation of the renogram curves, and quantitative parameters such as half-time of tracer washout may be supportive.

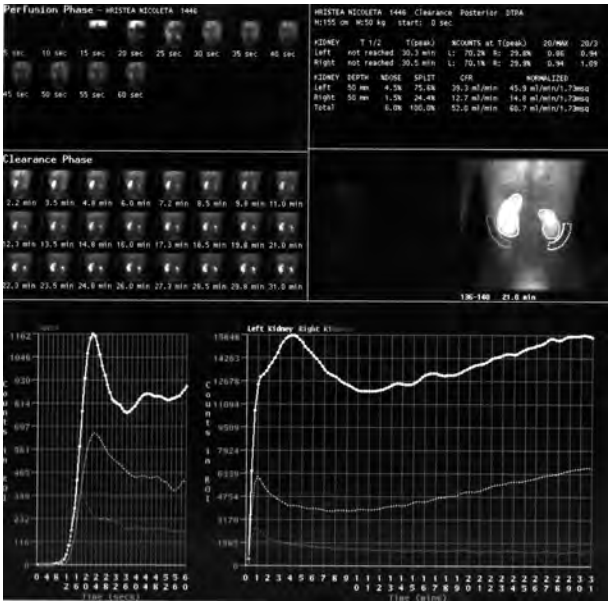


Fig. 3: Obstructive uropathy on left kydney

Renal transplantation

Renal scintigraphy plays an important role after renal transplantation. [15] It contributes to rapidly and accurately evaluating graft function, detecting surgical complications, and making differential diagnoses of medical complications. Only patients suspected of developing complications may undergo the imaging procedure; however, comparison with the previous study significantly aids in interpretation, and serial studies are more informative.

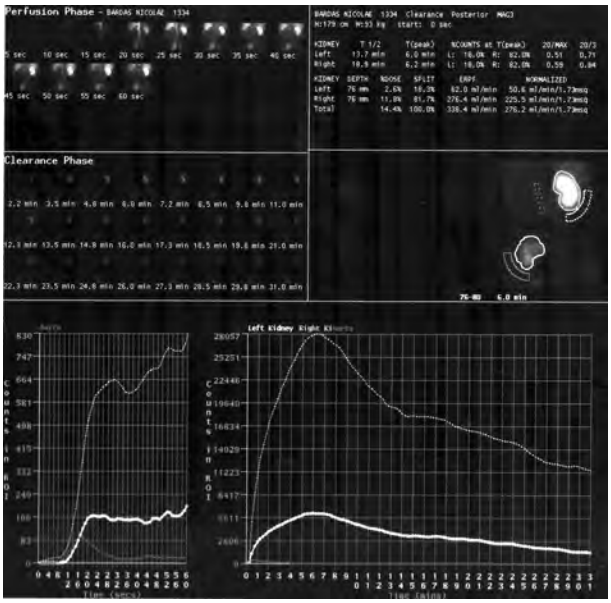


Fig. 4: Left renal transplant with hypofunction

MAG3 is the preferred agent for post-transplant observation because it provides highquality images in both the perfusion and function phases. Quantitative parameters are calculated for the evaluation of perfusion, clearance, and parenchymal transit time, and are used to assess acute tubular necrosis, acute rejection, and chronic rejection.Acute tubular necrosis is commonly present at the time of transplantation and is usually reversible without specific therapy. In chronic rejection, renal function is decreased but parenchymal transit remains relatively normal. Nephrotoxicity of drugs such as cyclosporine does not cause specific findings on renal scintigrams. Renal infarction and urine leak can be detected by renal scintigraphy.

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