

Furosemide for the diagnosis of complete or partial ureteropelvic junction obstruction

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Abstract

Furtive accumulation of the radiopharmaceutical in the urinary draining system as shown by routine renal tests, like technetium-99m-diethylenetriamine pentacetic acid, technetium-99m-mercaptalacetyltriglycine or technetium-99m-glucoheptonate renograms can be re-evaluated by administering a diuretic, like furosemide (FS) and obtaining post FS dynamic and static images. Urinary tract obstruction can thus be identified. Partial urinary tract obstruction, the effectiveness of stenting, the effectiveness of obstruction correcting surgery and retroperitoneal lymph nodes, may be diagnosed after FS induced diuresis. However, factors like loss of the compliance of the renal pelvis or the ureter, low renal function, renal immaturity in neonates and full or neurogenic bladder limit the diagnostic effectiveness of FS. Diuretic enhanced Doppler sonography and dynamic contrast-enhanced magnetic resonance imaging can also be used for the evaluation of partial or complete urinary tract obstruction. The FS induced diuresis procedure is compared to other related diagnostic techniques.

Introduction

Pooling of a radiotracer into renal pelvicalyceal system (PCS) is not easily evaluated, as it may be due to nephrolithiasis, renal neoplasm, retroperitoneal fibrosis, enlarged lymph node pressure, ureteric tuberculosis or to congenital ureteropelvic junction (UPJ) obstruction in neonates and children. The latter may be due to ureteral mucosa fold or to fibrous cords or iliac vessels superficially crossing and compressing UPJ [1]. The possibility of metastases at the UPJ even of a small size, not discerned into the "hot" huge area of the collected urine, cannot be excluded [2].

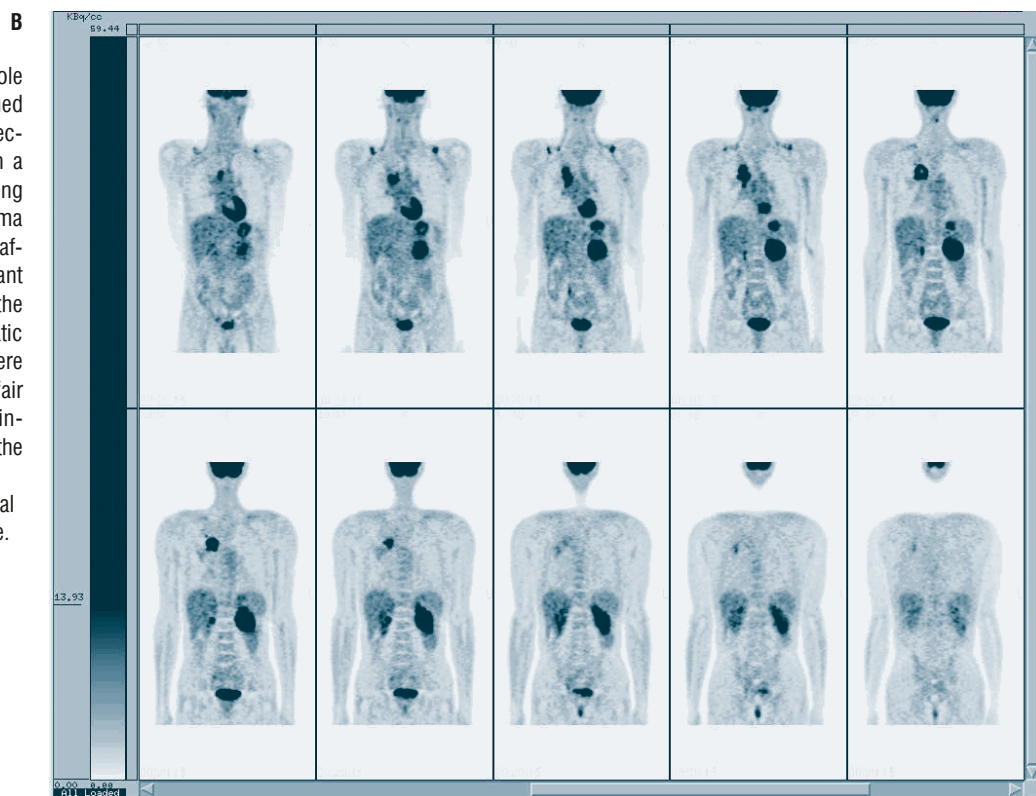
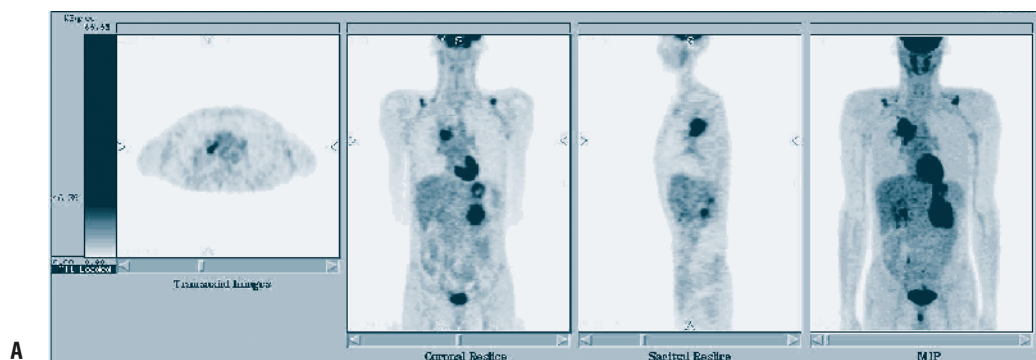
Radioactive accumulation into the PCS is observed during a renogram that can be performed by various radiopharmaceuticals like diethylenetriamine pentacetic acid (^{99m}Tc-DTPA), mercaptalacetyltriglycine (^{99m}Tc-MAG3) or glucoheptonate (^{99m}Tc-GH). Other radiopharmaceuticals that are normally excreted through the kidneys [3], such as ^{99m}Tc-diphosphonates, radiolabelled somatostatin receptor analogs, radiolabelled monoclonal antibodies, ^{99m}Tc-red blood cells and fluorine-18 fluorodeoxyglucose (¹⁸F-FDG), fluorine-18 fluorodopamine and fluorine-18 fluorothymidine can also identify accumulation of the radiopharmaceutical into the PCS [4, 5]. An unusual, randomly found, accumulation into the renal PCS should always be further investigated, as a neglected obstruction could be detrimental for the involved kidney. Experiments in rats

have shown that after ligation of the ureter and after total PCS obstruction, the inflow above ligation area will disappear within 15 days and the kidney will become non functional [6]. It has also been observed in rats that after partial ureteral obstruction, the glomerular filtration rate (GFR) of the involved kidney decreases initially, but later renal function remains stable till the natural death of the animal [7].

For the distinction between obstruction and dilatation of renal PCS, furosemide (FS) injection is routinely used (Fig. 1A and B, Fig. 2). Furosemide (4-chloro-2-(furan-2-ylmethylamino)-5-sulfamoylbenzoic acid) is a loop diuretic that inhibits sodium and chloride reabsorption in the proximal and distal tubules and in the Henle loop, thus increasing urine flow. The injection of FS is contraindicated in dehydrated and in hypotensive patients and may aggravate hypokalemia [8]. Furosemide is injected slowly over 1-2min, in a dose of 1mg/dL (max 20mg) in children [9] and in a dose of 40mg in adults, which may be increased in cases of high serum creatinine [10]. Furosemide has an estimated onset of action at about 30-60sec and a maximal effect at 15min [10]. Due to these characteristics and depending on the desired time of its maximal effect, there are three different time administration protocols (F+20, F-0 and F-15) [11-13]. It is suggested that when performing a whole body positron emission tomography (PET) scan with ¹⁸F-FDG and intend to inject FS for the evaluation of retroperitoneal nodes or pelvic metastases, the patient 30min prior to FS should be hydrated, by 20ml tap water/kg of body weight and acquisition should start 30min after FS injection [14]. On the other hand, if after scan acquisition renal PCS dilatation is observed, FS may be injected soon after the ¹⁸F-FDG study and rescanned 20-30min post- FS injection [15, 16].

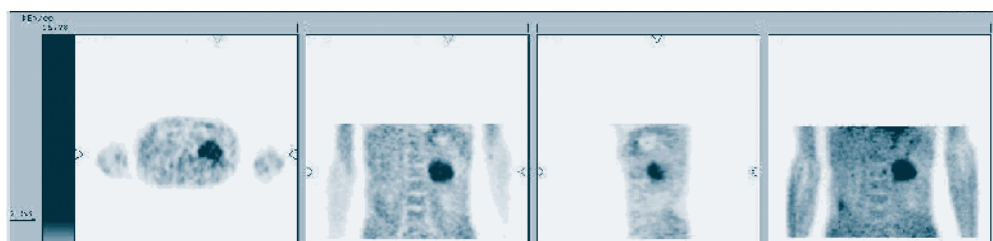
Normally the time-activity curve of the injected radiopharmaceutical rapidly reaches a sharp peak and then declines. Furosemide increases urine flow and accelerates the rate of the radiotracer washout. In an obstructed renal PCS, activity after FS will continue to accumulate or will stay at a plateau [17]. In a nonobstructed kidney or in a hydronephrotic one, FS will induce an increased urine flow (Fig. 3A and B).

Furosemide "resistance" usually implies a constant PCS obstruction and not a functional dilatation of the PCS. It indicates an obstruction either extrinsic, mural or intraluminal of urine flow. However, there are some limitations concerning the interpretation of such a finding. Obstructed and non-ob-



Figures 1A and B. A whole body ¹⁸F-FDG-PET performed 60min after intravenous injection of 444MBq ¹⁸F-FDG, in a 35 years old male suffering from a non small cell carcinoma of the right lung and treated after 2 cycles of neoadjuvant chemotherapy. Uptake in the primary lesion and metastatic adenopathy in the chest were revealed, in addition to a fair sized area of intensely increased ¹⁸F-FDG uptake in the left kidney.
 A: transverse, coronal, sagittal and maximal intensity picture.
 B: coronal slices.

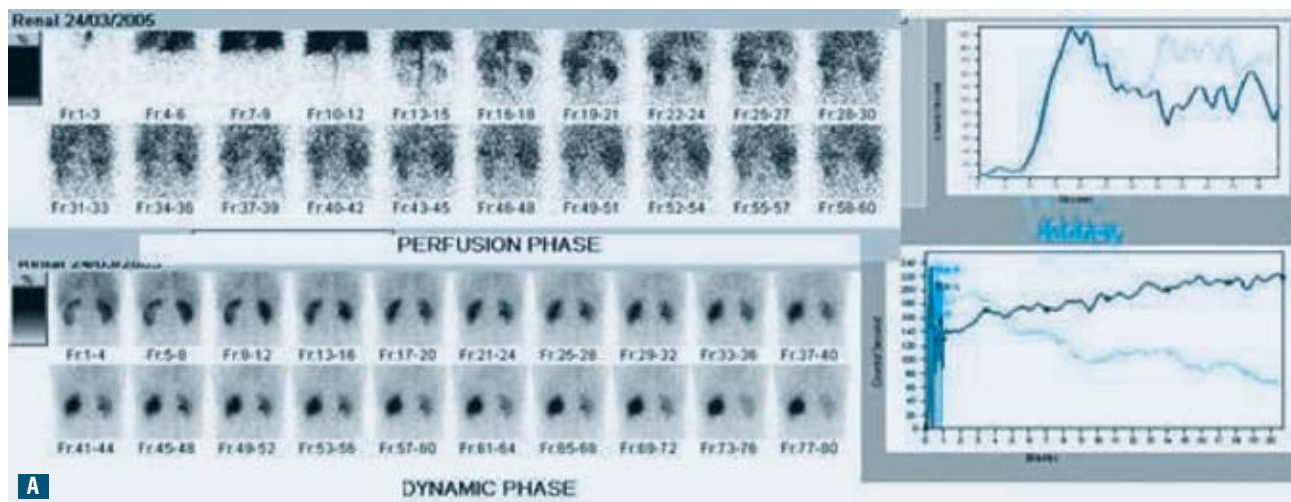
Figure 2. Following the procedure in Fig.1, intravenous FS was administered to rule out accumulation of ¹⁸F-FDG in the renal pelvicalyceal system and the patient was rescanned over the renal area. Uptake remained unchanged in the post-FS scan.



structed hydronephrosis can hardly be diagnosed when urine volume in the renal PCS increases, transit time delays and urine reservoir appears. Due to the urine reservoir effect non-obstructed cases of hydronephrosis may have an indeterminate response [18]. Additionally, if renal function is quite impaired, response to FS may be markedly diminished, leading to prolonged washout even if no obstruction is present. Thus, when GFR on the affected UPJ is less than 15ml/min or when there is neonatal functional immaturity, full or neurogenic urinary bladder, pelvic kidney or low-lying renal transplant, then

diuretic response is unreliable [10, 19].

It is known that, the best way to evaluate a hydronephrotic kidney with kidney function of less than 40%, and to calculate parameters such as tissue tracer transit (TTT) and response to FS, is to use ^{99m}Tc-MAG3 as radiopharmaceutical [20]. Delayed TTT may identify the need for treatment in order to preserve the function of the hydronephrotic kidney, while normal TTT may exclude the risk of renal insufficiency even in the presence of an abnormal response to FS or of a kidney function of less than 40% [20].

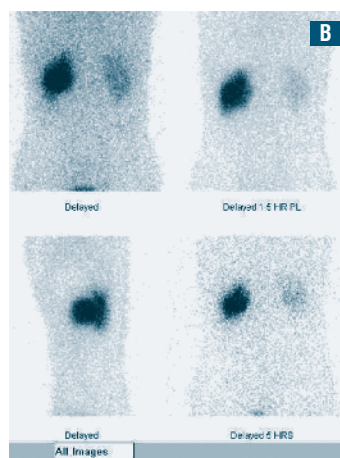


There are also other modalities for the evaluation of urinary tract obstruction. Ultrasonography is a sensitive method of identifying a dilated collecting system but can not reliably determine if dilatation is due to significant mechanical obstruction or merely nonobstructive hydronephrosis [20]. Diuretic enhanced Doppler sonography can be used as a second line test in cases of an indeterminate radionuclidic diuretic renogram, characterized by a half clearance time ($T_{1/2}$) between 15-20min. Kidneys with severe UPJ obstruction tend to have more elevated resistive indices (RI) during the cardiac cycle than the non-obstructed or equivocally obstructed ones [21, 22]. These indices are calculated by $RI = (\text{peak systolic velocity} - \text{end diastolic velocity}) / \text{peak systolic velocity}$, while pulsatility indices by $PI = (\text{peak systolic velocity} - \text{minimum diastolic velocity}) / \text{mean velocity}$.

Intravenous pyelography (IVP) shows findings between delayed filling, dilatation and decreased washout but this test is not as sensitive as radionuclidic renogram and administers higher doses of radioactivity to the patient [23]. Endoscopy, retrograde pyelography and CT scan can often identify the etiology of obstruction but do not provide functional information for the management of these patients [10]. Retrograde pyelography and CT scan also administer higher radiation absorption doses to the patients [23]. Dynamic contrast-enhanced MRI provides better information, concerning urinary tract anatomy, differential renal function estimation and urinary tract obstruction evaluation. This method is characterized by high sensitivity and high negative predictive value [24- 26].

Whitaker test first described in 1973 is the most sensitive test for the diagnosis of ureteropelvic obstruction but is rarely performed nowadays because it involves bladder catheterization and needle insertion into the renal pelvis under fluoroscopy [27].

In conclusion, a randomly found accumulation of any radiopharmaceutical in the UPJ may be further examined by FS administration for a possible intra- or extra- ureteric obstruction. Pitfalls of this test are mentioned. The related diagnostic value of ultrasonography, CT and MRI are discussed.



Figures 3A and B. A ^{99m}Tc -DTPA renogram demonstrating a greatly dilated PCS (A) with evidence of left sided renal drainage obstruction in the post-FS delayed images (B). The split renal function of the left kidney at the time of the study was relatively well maintained (42.9%) with estimated total GFR of 92.8ml/min. Differential diagnosis led to metastatic lesion obstruction.

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