The Role of PET Scanning in the Evaluation of Patients With Kidney Disease

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Patients with underlying kidney disease are often required to undergo imaging for a variety of purposes including diagnosis and prognosis. A test that is being increasingly used with for this group of patients is the positron emission test (PET) scan. In addition, combining the nuclear medicine technique (PET) with computed tomography scan allows additional imaging advantages over either alone. These imaging modalities are commonly used for a number of extrarenal indications (ie, cancer, coronary artery disease, central nervous system disease, infectious diseases, and others). They have also been used for diagnosis of acute tubulointerstitial nephritis, evaluation and management of retroperitoneal fibrosis, identifying infection within kidney and liver cysts, and distinguishing complex kidney cysts from kidney cancer in patients with underlying CKD. We will review PET scan utility in patients with kidney disease.

Key Words: Positron emission tomography, Acute tubulointerstitial nephritis, Retroperitoneal fibrosis, Renal cell cancer, Renal cysts

INTRODUCTION

Patients with kidney disease possess a large number of co-morbid conditions that may require some form of diagnostic imaging. As a result, clinicians frequently use various imaging modalities to evaluate patients with acute and CKD, those with cystic kidneys and renal masses, those with renovascular disease, and patients with various other problems that develop.[1] For example, kidney ultrasonography, computed tomography (CT) scanning, and sometimes magnetic resonance imaging (MRI) are used to examine for the presence of urinary obstruction, critical renal artery stenosis, renal vein thrombosis, and kidney infarction.[2]

Noninvasive imaging, such as gallium scanning, is also occasionally used in an attempt to diagnose acute tubulointerstitial nephritis (ATIN) in patients who are at high risk for a complication or refuse to undergo kidney biopsy.[3] In other settings, patients with kidney disease due to retroperitoneal fibrosis (RF) often undergo CT scan and MRI to facilitate diagnosis and guide subsequent management.[4] To the latter point, assessing for the presence or absence of active inflammation within fibrosing retroperitoneal tissue is important to guide therapy, yet it is poorly served by these imaging modalities.

Adequately diagnosing kidney cancer in patients with underlying CKD who have complex kidney cysts and small renal masses noted on ultrasonography presents a challenging problem for clinicians. CT scanning and MRI with intravenous contrast are generally less desirable due to the concern of acute kidney injury (AKI) and other complications associated with these agents in patients with underlying kidney disease.[1] Finally, patients with cystic kidney disease, primarily those with autosomal dominant polycystic kidney disease (ADPKD), may develop cyst infections that can be notoriously difficult to diagnose and distinguish from cyst hemorrhage or another process.[5]

A test that has gained some traction as a useful imaging modality for patients with certain types of kidney disease is the 2-[^{18}F] fluoro-2-deoxy-D glucose (^{18}F-FDG) positron emission tomography (PET) scan, either alone or combined with CT scan (PET/CT scan). In current times, these modalities are used predominantly in the clinical arena for imaging patients with suspected or known malignancy including initial diagnosis, surveillance for metastases, and measuring efficacy of therapy.[6] Other uses include evaluation of patients with underlying coronary artery disease, infectious diseases, and those with central nervous system disorders, such as tumors, seizures, and infections.[7,8] In addition, PET and PET/CT scanning are used to map normal human brain and heart function.[9] Table 1 notes some of the uses of PET scanning in clinical practice.

This review will focus on the use of PET scanning in 4 entities in clinical nephrology: (1) ATIN; (2) RF; (3) kidney and liver cysts in patients with ADPKD; and (4) complex cysts/small renal masses and kidney cancer in patients with CKD.

PET AND PET/CT SCAN

PET is a nuclear, functional imaging technique that is used to evaluate metabolic processes within the body. The system is designed to detect pairs of gamma rays emitted indirectly by a positron-emitting radionuclide, which is introduced into the body on a biologically active molecule.[10] This radionuclide is a tracer that highlights the metabolically active areas within organs and tissues. Tracers also provide information about blood flow and tissue oxygen consumption. Three-dimensional images of tracer concentration within the body are then constructed by computer analysis. The biologically active molecule often used for PET is FDG, an analogue of glucose.

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Concentrations of FDG imaged typically indicate tissue metabolic activity as it corresponds to the regional glucose uptake by cells. As an example, PET scanning using FDG as the tracer is most commonly used and currently is a standard of care in the diagnosis and management of cancer.

Combined PET/CT scan is an imaging technique that uses a device that combines in a single gantry system both a PET scanner and a CT scanner, so that images acquired from both devices can be taken sequentially, in the same session, and combined into a single superposed or co-registered image.[11,12] Using this technique, PET obtained functional imaging, which depicts the spatial distribution of metabolic or biochemical activity in the body can be more precisely aligned or correlated with CT-generated anatomic imaging.[11,12] Thus, 2- and 3-dimensional image reconstruction may be rendered as a function of the common software and control system.

The PET/CT scan has clearly altered the ability of clinicians to diagnose and manage many medical conditions by melding precise anatomic localization with functional imaging. To this point, in current, the practice of medicine, the availability of PET/CT scan is rapidly changing the approach to pre-surgery mapping, radiation therapy, and cancer staging.[11,12] As a result, many centers are gradually abandoning conventional PET devices and substituting them by PET-CT scanners.

A disadvantage of PET/CT scanning is the greater cost compared with other tests; however, it does offer an advantage, in that it provides information normally required by 2 separate imaging modalities. Another barrier to more widespread use of PET-CT imaging is the difficulty of producing and transporting the short-lived radiopharmaceuticals.[11,12] For example, the $T_{1/2}$ of radioactive ^{18}F, which is used to trace glucose metabolism using FDG, is 2 hours only. In addition, production requires a relatively costly cyclotron and a production line for the radiopharmaceuticals.

CLINICAL SUMMARY

- Positron emission test (PET) scan, especially when combined with computed tomography (CT scan), allows imaging advantages in patients with kidney disease. Combined PET/CT scan has been used anecdotally for diagnosis of acute tubulointerstitial nephritis.
- PET scan appears to provide information about the metabolic activity of retroperitoneal fibrosis, which may guide treatment decisions.
- Combined PET/CT scan provides useful information for identifying infection within kidney and liver cysts in patients with ADPKD.
- Combined PET/CT scan helps distinguish complex kidney cysts from kidney cancer in patients with underlying CKD.

PATIENTS WITH ACUTE TUBULOINTERSTITIAL NEPHRITIS

A noninvasive imaging test, used primarily to evaluate malignant disease, has been recently used to diagnose ATIN.[13] Whereas kidney and CT scan may show increased kidney size and enhanced echogenicity in patients with underlying ATIN, the findings are quite nonspecific. In fact, these tests are best used as modalities to evaluate for hydronephrosis, nephrolithiasis, cysts, and masses within the kidneys.[14] A test that has been used to noninvasively evaluate for ATIN is the gallium scan. Based on the premise that gallium binds lactoferrin, which is expressed on white blood cell surfaces and also released into surrounding tissue by these cells,[3,15] it seems rational that patient with ATIN (and an inflammatory interstitial infiltrate) would "light up" with gallium. However, this imaging test turns out to have unacceptable sensitivity and specificity.[3,15,16] Many non-ATIN kidney disorders are associated with a positive gallium scan, whereas ATIN does not uniformly test positive with gallium scintigraphy.[3,15,16] Thus, other imaging modalities must be evaluated.

A single publication noted a positive PET/CT scan in 2 patients with severe AKI due to biopsy-proved ATIN and a negative PET scan in a third patient with AKI (without ATIN).[13] One of the patients with ATIN had a negative gallium scan, suggesting that PET/CT scan was superior to gallium scintigraphy. In a third patient with severe AKI due to biopsy-proved crescentic glomerulonephritis, the FDG-PET scan was negative. Repeat FDG-PET scans were negative in the 2 patients with ATIN after treatment and clinical resolution of kidney injury. Our modest personal experience with this test has been optimistic with FDG-PET/CT scan positive (Fig 1) in the setting of biopsy-proved drug-induced AKI. Uptake of tracer in the setting of ATIN is based on the premise that FDG accumulates not only in tumor cells but also in the metabolically lymphocytes, macrophages, neutrophils, and fibroblasts of inflammatory lesions.[13] Thus, this modality should undergo further study to judge its true utility (sensitivity and specificity) for diagnosis of ATIN.

PATIENTS WITH RETROPERITONEAL FIBROSIS

RF consists of a group of relatively rare diseases, which are characterized by proliferation of fibro-inflammatory tissue often surrounding the infrarenal portion of the abdominal aorta (Fig 2), inferior vena cava, and iliac vessels.[17-19] The fibrosing tissue may extend into neighboring structures, including the ureters, where it causes AKI by impairing ureteral peristalsis and promoting urinary obstruction.[17-19]

The idiopathic form of RF accounts for more than two-thirds of cases, whereas the remaining causes are due certain types of drugs, such as the ergot alkaloid derivatives and β blockers and malignancies including various metastatic tumors, lymphoma, retroperitoneal sarcoma, and carcinoid tumor.[17-20] Other secondary causes of RF include tissue invasive infections, such as tuberculosis, histoplasmosis, and actinomycosis, major abdominal surgery, retroperitoneal hemorrhage/hematoma, and radiation therapy.[17-21] Other potential causes include a