

University of Groningen

F-18-FDG PET/CT in Autosomal Dominant Polycystic Kidney Disease Patients with Suspected Cyst Infection

Pijl, Jordy P.; Glaudemans, Andor W. J. M.; Slart, Riemer H. J. A.; Kwee, Thomas C.

Published in:
Journal of Nuclear Medicine

DOI:
[10.2967/jnumed.117.199448](https://doi.org/10.2967/jnumed.117.199448)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2018

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Pijl, J. P., Glaudemans, A. W. J. M., Slart, R. H. J. A., & Kwee, T. C. (2018). F-18-FDG PET/CT in Autosomal Dominant Polycystic Kidney Disease Patients with Suspected Cyst Infection. *Journal of Nuclear Medicine*, 59(11), 1734-1741. <https://doi.org/10.2967/jnumed.117.199448>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

¹⁸F-FDG PET/CT in Autosomal Dominant Polycystic Kidney Disease Patients with Suspected Cyst Infection

Jordy P. Pijl¹, Andor W.J.M. Glaudemans¹, Riemer H.J.A. Slart^{1,2}, and Thomas C. Kwee¹

¹Medical Imaging Center, Department of Radiology, Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; and ²Department of Biomedical Photonic Imaging (BMPI), University of Twente, Enschede, The Netherlands

The objective of this study was to determine the value of ¹⁸F-FDG PET/CT for diagnosing renal or hepatic cyst infection in patients with autosomal dominant polycystic kidney disease (ADPKD).

Methods: This retrospective, single-center study included all patients who had ADPKD and underwent ¹⁸F-FDG PET/CT because of suspected cyst infection between 2010 and 2017. **Results:** Thirty ¹⁸F-FDG PET/CT scans of 30 individual patients were included; 19 of them had positive results for cyst infection. According to a previously established clinical and biochemical reference standard, ¹⁸F-FDG PET/CT achieved a sensitivity of 88.9%, a specificity of 75.0%, a positive predictive value of 84.2%, and a negative predictive value of 81.8% for the diagnosis of cyst infection. In 5 cases, ¹⁸F-FDG PET/CT suggested that the symptoms could be explained by a different pathologic process, including pneumonia ($n = 1$), generalized peritonitis ($n = 1$), pancreatitis ($n = 1$), colitis ($n = 1$), and cholangitis ($n = 1$). The total duration of the hospital stay and the duration between the ¹⁸F-FDG PET/CT scan and hospital discharge for patients with ¹⁸F-FDG PET/CT scan results that were positive for cyst infection were significantly longer than those for patients with negative scan results ($P = 0.005$ and $P = 0.009$, respectively). Creatinine levels were significantly higher in patients with ¹⁸F-FDG PET/CT scan results that were positive for cyst infection than in patients with negative scan results ($P = 0.015$). Other comparisons of clinical parameters (age, sex, presence of fever [$>38.5^{\circ}\text{C}$] for more than 3 d, abdominal pain, history of solid-organ transplantation and nephrectomy, and immune status), laboratory values (C-reactive protein level, leukocyte count, and estimated glomerular filtration rate), and microbiologic test results (blood and urine cultures) were not significantly different ($P = 0.13$ – 1.00) in patients with positive and negative ¹⁸F-FDG PET/CT scan results. **Conclusion:** ¹⁸F-FDG PET/CT is a useful imaging modality for the evaluation of patients with ADPKD and suspected cyst infection.

Key Words: infectious disease; PET/CT; kidney; ADPKD; cyst; infection

J Nucl Med 2018; 59:1734–1741

DOI: 10.2967/jnumed.117.199448

With a reported prevalence of 1 in 400 to 1,000, autosomal dominant polycystic kidney disease (ADPKD) is one of the most common inherited monogenic disorders worldwide (1–3). Patients with the causative mutation in either the PKD1 gene (85% of patients) or the PKD2 gene (15% of patients) develop cysts in multiple organs, mostly affecting the kidneys (1–3). Liver cysts are also common, particularly with increasing age, but often remain asymptomatic (1–3). Cyst infection is a common complication in patients with ADPKD. It has been estimated that 30%–50% of patients will develop at least 1 renal cyst infection during their lifetimes (4), and approximately 10% of hospitalizations in ADPKD patients are due to cyst infection (5). Prompt diagnosis of cyst infections is important, as such infections require specific treatment (3). The fact that most conventional antibiotics are hydrophilic substances prevents them from penetrating the cystic walls; the consequence is ineffective treatment of cyst infections (3). Eradication of these infections therefore requires specific lipophilic antibiotics, such as fluoroquinolones and trimethoprim (3). Timely treatment is important for preventing infection progression, abscess formation, bacteremia, and sepsis.

Diagnosis of cyst infection in patients with ADPKD remains challenging. Cyst fluid analysis by means of puncture is the diagnostic gold standard but is rarely performed because of the risk of complications, such as contamination of adjacent cysts, sepsis, bleeding, or even death (6). Moreover, identifying which cyst is infected is difficult, and often an infected cyst cannot be accessed percutaneously (7). Conventional radiologic modalities, such as ultrasonography, CT, and MRI, are limited in diagnosing infection (6–8). Iodinated CT contrast agents and gadolinium-based MRI contrast agents can be contraindicated in patients with impaired renal function because of the potential risks of nephrotoxicity and nephrogenic systemic fibrosis, respectively (8).

¹⁸F-FDG PET, on the other hand, may be a potentially useful imaging technique for detecting cyst infection. Activated inflammatory cells (such as macrophages and neutrophils) at a site of infection accumulate ¹⁸F-FDG (9), which can be visualized by PET with a high contrast ratio and anatomically pinpointed with concomitantly acquired CT. Also, the administration of ¹⁸F-FDG is not contraindicated in patients with impaired renal function.

Previous studies reported ¹⁸F-FDG PET/CT to be useful in ADPKD patients (Table 1) (5,10–15). However, because of few included patients or unclear reporting of diagnostic power in these studies, there is still no consensus on the widespread use of ¹⁸F-FDG PET/CT in this setting. Recent European Association of Nuclear Medicine guidelines still described the use of ¹⁸F-FDG

Received Jan. 18, 2018; revision accepted Mar. 28, 2018.

For correspondence or reprints contact: Jordy P. Pijl, Department of Radiology, Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, Hanzeplein 1, P.O. Box 30.001, 9700 RB Groningen, The Netherlands.

E-mail: j.p.pijl@umcg.nl

Published online Apr. 13, 2018.

COPYRIGHT © 2018 by the Society of Nuclear Medicine and Molecular Imaging.

TABLE 1
Literature on the Diagnosis of Cyst Infection in Polycystic Patients

Study	No. of included patients	No. of included scans	No. of PET result–positive cyst infections	Sensitivity	Specificity
12*	Unknown	28	8	80% (8/10)	89% (16/18)
11*	24	32	14	78% (14/18)	100% (14/14)
10*	28	Unknown	19	95% (19/20)	Unknown
14†	10	10	6	Unknown	Unknown
13*	24	27	11	85% (11/13)	86% (12/14)
5*	8	8	8	100% (8/8)	Unknown
15†	3	7	5	Unknown	Unknown

*Reference standard of Sallée et al. (5) was used to confirm cyst infection found on ^{18}F -FDG PET/CT.

†Other clinical criteria and follow-up were used as reference standard for diagnosing cyst infection on ^{18}F -FDG PET/CT.

PET/CT for the evaluation of potentially infected liver and kidney cysts in polycystic disease as insufficiently evidence-based (16).

The aim of this study was to determine the diagnostic value of ^{18}F -FDG PET/CT in ADPKD patients with clinically suspected cyst infection.

MATERIALS AND METHODS

Study Design and Patients

The local institutional review board approved this retrospective, single-center study and waived the requirement for written informed consent. All patients who had ADPKD and underwent ^{18}F -FDG PET/CT because of suspected cyst infection between August 2010 and April 2017 were potentially eligible for inclusion. Inclusion criteria were diagnosis of ADPKD according to established criteria (17), clinically suspected cyst infection, and availability of ^{18}F -FDG PET/CT imaging that was performed to diagnose cyst infection. Exclusion criteria were no diagnosis of ADPKD, ^{18}F -FDG PET/CT that was not performed because of potential cyst infection, and specific missing clinical and laboratory data. The presence of fever, the presence of abdominal pain, and C-reactive protein (CRP) level were used as part of the reference standard (as explained later); hence, the results of the ^{18}F -FDG PET/CT scan could not be tested against the reference standard in the absence of these data. If a patient underwent multiple ^{18}F -FDG PET/CT scans because of suspected cyst infection, then the ^{18}F -FDG PET/CT scan first performed was selected and the subsequent scans were excluded.

Patient Record Review

The medical records of the included patients were reviewed for relevant clinical data (age, sex, presence of fever [$>38.5^\circ\text{C}$] for more than 3 d, abdominal pain, history of solid-organ transplantation and nephrectomy, immune status, duration of hospital stay, and antibiotic use), laboratory values (CRP level, leukocyte count, creatinine level, estimated glomerular filtration rate, and microbiologic tests [blood and urine cultures]), and the results of all other imaging studies that were performed during hospitalization for suspected cyst infection. All laboratory values were measured within 2 d of the ^{18}F -FDG PET/CT scan.

^{18}F -FDG PET Acquisition

Patients fasted for a minimum of 6 h, and blood glucose concentrations were confirmed to be less than 11 mmol/L before ^{18}F -FDG (3 MBq/kg of body weight) was administered intravenously. Approximately 60 min after ^{18}F -FDG administration, PET scanning was performed from mid-

thigh to the cranial vertex using a resEARCh 4 Life–accredited integrated PET/CT system (Biograph mCT 64-slice PET/CT; Siemens) at 3 min/bed position. Low-dose CT was performed for attenuation correction and anatomic mapping at the following settings: tube voltage of 100 kV, gantry rotation time of 0.5 s, pitch factor of 1.5, automated exposure control switched on during all acquisitions (CARE Dose 4D; Siemens) with a quality reference effective tube current–time product of 30 mAs, an average tube current of 90 mAs, and an effective tube current–time product of 30 mAs.

Data acquisition and reconstruction were performed in accordance with European Association of Nuclear Medicine guidelines (18). In 4 patients, concomitant full-dose CT of the abdomen was performed with a constant tube potential of 100 or 120 kV and an automatic adjustment of mAs in the z-direction, with scanning in the portal venous phase in 3 patients and without the administration of intravenous contrast agent in 1 patient.

^{18}F -FDG PET Interpretation

^{18}F -FDG PET/CT scans were interpreted by board-certified nuclear medicine physicians using Syngo.Via software (Siemens Healthcare) as part of routine clinical care. Each scan was reevaluated by another reader who was unaware of the original ^{18}F -FDG PET/CT interpretations, other imaging, and clinical, laboratory, and microbiologic tests. Renal or hepatic cysts with higher ^{18}F -FDG uptake in cyst walls than in surrounding residual parenchyma (excluding physiologic urinary excretion), heterogeneous ^{18}F -FDG uptake in the cyst wall (including focal or multifocal increased uptake), or diffuse signal accumulation within the cyst after the exclusion of cyst hemorrhage by CT were considered positive for infection. Extrarenal and extrahepatic organs were also evaluated for pathologic foci of ^{18}F -FDG uptake that might represent inflammation or infection. The low-dose CT part of the ^{18}F -FDG PET/CT scan was reviewed to exclude intracystic bleeding, defined as the presence of hyperattenuating (>50 Hounsfield units) intracystic material. This second reading was then compared with the original ^{18}F -FDG PET/CT reports to reveal any discrepancies.

Reference Standard

Given the lack of cyst aspiration and subsequent microbiologic testing for previously mentioned reasons, a composite reference standard based on the criteria of Sallée et al. (5,10–13) was used for cyst infection. According to these criteria (5,10–13), hepatic or renal cyst infection was (likely) considered to be present when a patient met all 5 of the following criteria: fever exceeding 38.5°C for more than

3 d, presence of abdominal pain, CRP level of greater than 50 mg/L, absence of any recent intracystic bleeding or other known causes of fever, and favorable outcome with antibiotic treatment.

The results of the ^{18}F -FDG PET/CT scans were considered to be true-positive for cyst infection when the patients met all 5 criteria and the scans showed signs of cyst infection, as described earlier. When the patients met all 5 criteria but their ^{18}F -FDG PET/CT scans did not reveal signs of cyst infection, then the results of the scans were considered to be false-negative.

Statistical Analysis

Continuous variables were checked for normal distribution using Kolmogorov–Smirnov tests. Data were presented as mean \pm SD (normally distributed) or median and interquartile range (non-normally distributed). The sensitivity, specificity, positive predictive value, and negative predictive value of ^{18}F -FDG PET/CT for the diagnosis of hepatic or renal cyst infection were calculated, along with 95% CIs. Differences in clinical parameters (age, sex, presence of fever [$>38.5^\circ\text{C}$] for more than 3 d, abdominal pain, history of solid-organ transplantation and nephrectomy, immune status, and duration of hospital stay), laboratory values (CRP level, leukocyte count, creatinine level, and estimated glomerular filtration rate), and microbiologic tests (blood and urine cultures) between ^{18}F -FDG PET/CT–positive and ^{18}F -FDG PET/CT–negative results for hepatic or renal cyst infection (excluding patients with ^{18}F -FDG–avid foci elsewhere) and between all ^{18}F -FDG PET/CT–positive and all ^{18}F -FDG PET/CT–negative cases (including patients with ^{18}F -FDG–avid foci outside the liver and kidneys) were assessed using 2-tailed unpaired *t* tests for normally distributed data, Mann–Whitney tests for non-normally distributed data, and Fisher tests for dichotomous data. *P* values of less than 0.05 were considered statistically significant. Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS), version 25 (IBM SPSS).

RESULTS

^{18}F -FDG PET/CT Scans and Patients

Sixty-seven ^{18}F -FDG PET/CT scans were potentially eligible for inclusion. However, 21 ^{18}F -FDG PET/CT scans were excluded because they did not fulfill the criteria for ADPKD; 11 ^{18}F -FDG PET/CT scans were excluded because they were from patients for whom previous scans had already been included; and 5 ^{18}F -FDG PET/CT scans were excluded because clinical, laboratory, and microbiologic data were missing as a result of transfer of patients to another hospital. Finally, 30 ^{18}F -FDG PET/CT scans from 30 individual patients were included. These 30 scans were performed for 15 men and 15 women, with a median age of 61 y (Table 2). Most ^{18}F -FDG PET/CT scans were performed for patients with a solid-organ transplant (20/30; 67%), most patients were immunocompromised (26/30; 87%), and most patients had positive blood or urine culture results (22/30; 73%) (Table 3). The mean duration of the hospital stay was 12.6 d.

Main ^{18}F -FDG PET/CT Findings

In 24 of 30 cases (80%), a focus of infection was identified on the ^{18}F -FDG PET/CT scan. These foci included cyst infection ($n = 19$), cholangitis ($n = 1$), pancreatitis ($n = 1$), pneumonia ($n = 1$), colitis ($n = 1$), and generalized peritonitis ($n = 1$). In all 24 cases, the focus of infection found on ^{18}F -FDG PET/CT led to or confirmed the main clinical diagnosis for the patient. In the remaining 6 cases, with negative ^{18}F -FDG PET/CT scan results, the final “diagnoses” were urinary tract infection ($n = 3$); on the basis of positive urine culture results), fever of unknown origin ($n = 2$); on the

basis of a lack of any positive test results), and urosepsis ($n = 1$; on the basis of blood cultures).

Diagnostic Performance of ^{18}F -FDG PET/CT

The results of 19 of 30 ^{18}F -FDG PET/CT scans (63%) were judged positive for cyst infection (11 renal cyst infections and 8 hepatic cyst infections), with no discrepancies between the original reports and the reevaluation. There were no cases of intracystic bleeding. According to the reference standard, ^{18}F -FDG PET/CT provided 16 true-positive results, 3 false-positive results (due to a lack of abdominal pain or fever), 9 true-negative results, and 2 false-negative results for cyst infection. These data resulted in a sensitivity of 88.9% (95% CI: 65.3%–98.6%), a specificity of 75.0% (95% CI: 42.8%–94.5%), a positive predictive value of 84.2% (95% CI: 66.4%–93.5%), and a negative predictive value of 81.8% (95% CI: 53.9%–94.5%) for ^{18}F -FDG PET/CT in the diagnosis of cyst infection in ADPKD patients. Representative examples are shown in Figures 1 and 2.

In 5 of 30 ^{18}F -FDG PET/CT scans, an infectious focus other than cyst infection was identified. A case of cholangitis found on ^{18}F -FDG PET/CT was confirmed by MR cholangiopancreatography, endoscopic retrograde cholangiopancreatography, and clinical findings. In another patient, pancreatitis found on ^{18}F -FDG PET/CT was confirmed by endoscopic retrograde cholangiopancreatography, MRI, and laboratory values (markedly increased serum amylase and lipase levels). The case of pneumonia was confirmed by chest radiography, colitis in another patient was confirmed by microbiologic cultures and clinical findings, and generalized peritonitis in yet another patient was confirmed by laparotomy. Given these 5 true-positive results, ^{18}F -FDG PET/CT achieved an overall sensitivity of 91.3% (95% CI: 72.0%–98.9%) and a positive predictive value of 87.5% (95% CI: 74.7%–94.3%).

Alternative Imaging for Cyst Infection

Around the time of the ^{18}F -FDG PET/CT scan, abdominal ultrasonography was performed for 8 patients, full-dose contrast-enhanced CT was performed for 4 patients, and MRI was performed for 2 patients. According to the reference standard (5,10–13), ultrasonography yielded 1 true-negative and 7 false-negative cases of cyst infection. Full-dose contrast-enhanced CT yielded 1 true-negative and 3 false-negative results, and MRI yielded 2 true-negative results.

^{18}F -FDG PET/CT Status Versus Clinical, Laboratory, and Microbiologic Parameters

Various clinical, laboratory, and microbiologic data are summarized in Tables 2 and 3. Interestingly, the total duration of the hospital stay and the duration between the ^{18}F -FDG PET/CT scan and discharge from the hospital for patients with positive ^{18}F -FDG PET/CT scan results were significantly longer ($P = 0.005$ and $P = 0.009$, respectively) than those for patients with negative ^{18}F -FDG PET/CT scan results. Creatinine levels were significantly higher ($P = 0.015$) in patients with ^{18}F -FDG PET/CT scan results that were positive for cyst infection. All other comparisons of clinical, laboratory, and microbiologic parameters were not significantly different ($P = 0.13$ – 1.00) between patients with ^{18}F -FDG PET/CT scan–positive results and those with ^{18}F -FDG PET/CT scan–negative results.

Antibiotic Use

The antibiotic regimen for 63% of patients (12/19) in whom cyst infection was found on ^{18}F -FDG PET/CT was maintained or

TABLE 2
Clinical Parameters for All Included Patients and Comparison of Patients with Positive and Negative Results on ¹⁸F-FDG PET/CT

Parameter	All patients (n = 30)	No. of patients with any infectious focus found on ¹⁸ F-FDG PET/CT (n = 24)	No. of patients with no infectious focus found on ¹⁸ F-FDG PET/CT (n = 6)	No. of patients with cyst infection found on ¹⁸ F-FDG PET/CT (n = 19)*	P value for:	
					Any infectious focus vs. no infectious focus found on ¹⁸ F-FDG PET/CT	Patients with cyst-positive vs. cyst-negative results on ¹⁸ F-FDG PET/CT
Age (y)	61.0 (9.0) [†]	61.5 (11.0) [†]	60.0 (7.0) [†]	57.5 (10.0) [†]	0.516 [†]	0.975 [†]
Sex (M/F)	15/15	11/13	4/2	7/12	0.651 [§]	0.35 [§]
Presence of fever (>38.5°C) for >3 d (yes/no)	26/4	21/3	5/1	17/2	1.0 [§]	1.0 [§]
Presence of abdominal pain (yes/no)	25/5	20/4	5/1	17/2	1.0 [§]	1.0 [§]
Solid-organ transplant (yes/no)	20/10	14/10	6/0	10/9	0.074 [§]	0.057 [§]
Kidney	17	14	6	10		
Liver	2	1	1	0		
Nephrectomy performed	9	8	1	7	0.633 [§]	0.624 [§]
Unilateral	6	6	0	6		
Bilateral	3	2	1	1		
Immunocompromised (yes/no)	26/4	20/4	6/0	15/4	0.557 [§]	0.54 [§]
Use of immunosuppressants	20	14	6	10		
Dialysis	6	6	0	5		
Duration of hospital stay (d)						
Total	12.6 ± 10.2	14.3 ± 10.9 ^{,¶}	6.3 ± 1.5	15.2 ± 11.6 ^{,¶}	0.003 ^{**}	0.005 ^{**}
Between admission and PET/CT scan	4.89 ± 4.0	5.5 ± 4.4 ^{,¶}	3.7 ± 1.8	5.1 ± 4.3 ^{,¶}	0.201 ^{**}	0.256 ^{**}
Between PET/CT scan and discharge	7.7 ± 9.0	9.1 ± 9.7 ^{,¶}	2.7 ± 1.9	10.1 ± 10.4 ^{,¶}	0.122 ^{**}	0.009 ^{**}

[†]Eleven had ¹⁸F-FDG-avid renal cyst and 8 had ¹⁸F-FDG-avid hepatic cyst.

[‡]Median, with interquartile range in parentheses.

[§]Determined by Mann-Whitney test.

^{||}Determined by Fisher test.

[¶]Mean ± SD.

^{**}Only 22 of 24 ¹⁸F-FDG PET/CT scans with results that were positive for cyst infection were included (2 scans were performed after hospital discharge).

^{††}Only 18 of 19 ¹⁸F-FDG PET/CT scans with results that were positive for cyst infection were included (1 scan was performed after hospital discharge).

^{†††}Determined by unpaired *t* test.

TABLE 3
Laboratory Values for All Included Patients and Comparison of Patients with Positive and Negative Results on ¹⁸F-FDG PET/CT

Parameter	All patients (n = 30)	Any infectious focus found on ¹⁸ F-FDG PET/CT (n = 24)		Cyst infection found on ¹⁸ F-FDG PET/CT (n = 19)*	P value for:	
		No infectious focus found on ¹⁸ F-FDG PET/CT (n = 6)	Any infectious focus vs. no infectious focus found on ¹⁸ F-FDG PET/CT		Any infectious focus vs. no infectious focus found on ¹⁸ F-FDG PET/CT	Patients with cyst-positive vs. cyst-negative results on ¹⁸ F-FDG PET/CT
CRP (mg/dL)	95 (82) [†]	106 (95) [†]	109 (66) [†]	106 (91) [†]	0.917 [‡]	0.899 [‡]
CRP of >50 mg/dL (yes/no)	29/1	23/1	6/0	18/1	1.0 [§]	1.0 [§]
Leukocyte count (g/L)	8.9 (5.3) [†]	8.9 (7.5) [†]	9.0 (4.6) [†]	8.9 (8.4) [†]	0.659 [‡]	0.702 [‡]
Creatinine (μmol/L)	253 ± 246	283 ± 264	121 ± 52	307 ± 282	0.011 [¶]	0.015 [¶]
eGFR (mL/min/1.73 m ²)	48 (45) [†]	40 (51) [†]	55 (37) [†]	35 (51) [†]	0.144 [‡]	0.125 [‡]
Positive blood culture (yes/no)	12/18	8/16	4/2	6/13	0.184 [§]	0.175 [§]
<i>Escherichia coli</i>	5	3	2			
<i>Enterobacter faecalis</i>	2	2	0			
Other	5	3	2			
Positive urine culture (yes/no)	17/13	14/10	3/3	13/6	1.0 [§]	0.630 [§]
<i>Escherichia coli</i>	8	6	2			
<i>Klebsiella pneumoniae</i>	4	4	0			
Other	5	4	1			

*Eleven had ¹⁸F-FDG-avid renal cyst and 8 had ¹⁸F-FDG-avid hepatic cyst.

[†]Median, with interquartile range in parentheses.

[‡]Determined by Mann-Whitney test.

[§]Determined by Fisher test.

^{||}Mean ± SD.

[¶]Determined by unpaired *t* test.

eGFR = estimated glomerular filtration rate.

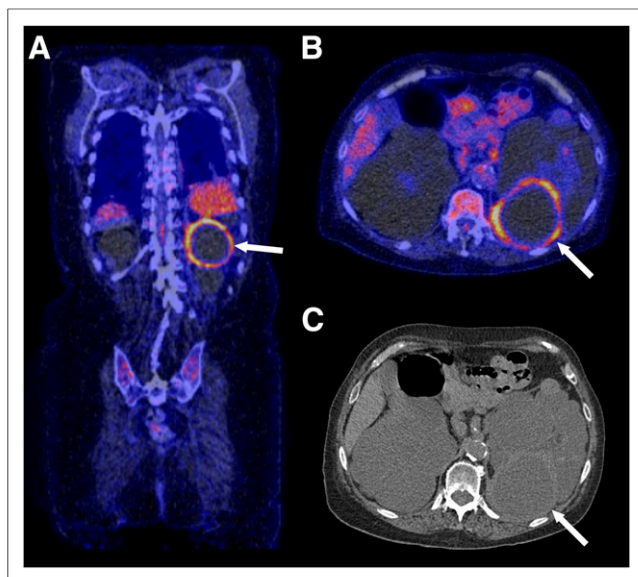


FIGURE 1. A 79-y-old woman who had ADPKD and whose ^{18}F -FDG PET/CT results were positive for renal cyst infection. (A and B) Coronal (A) and axial (B) fused ^{18}F -FDG PET/CT showed ^{18}F -FDG-avid cyst wall in left kidney (arrows), indicative of infection. (C) Axial CT at same level showed cyst (arrow) with slightly thickened and hyperattenuating wall. Criteria of Sallée et al. (5,10–13) for cyst infection were also met in this patient.

changed to antibiotics favorable for treating cyst infection (Table 4). The same was done in 50% of patients (3/6) in whom no infection was found on ^{18}F -FDG PET/CT. When a focus of infection other than cyst infection was found on ^{18}F -FDG PET/CT, antibiotic therapy was switched to the better option on the basis of clinical and

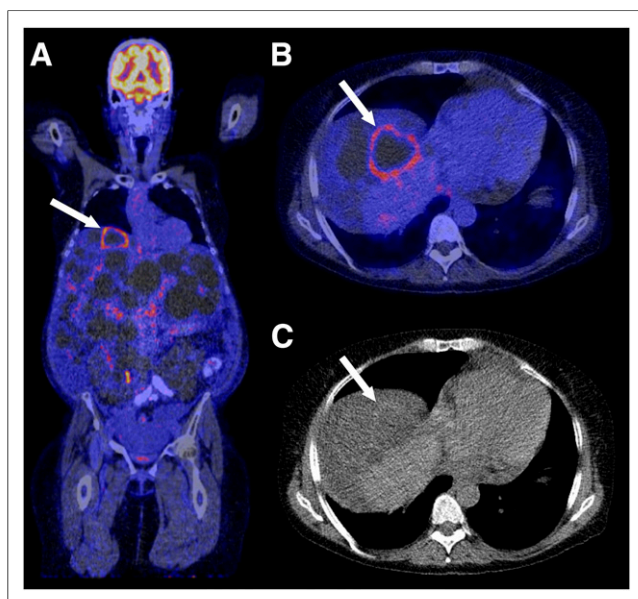


FIGURE 2. A 56-y-old woman who had ADPKD and whose ^{18}F -FDG PET/CT results were positive for hepatic cyst infection. (A and B) Coronal (A) and axial (B) fused ^{18}F -FDG PET/CT showed ^{18}F -FDG-avid cyst wall in liver segment 8 (arrows), indicative of infection. (C) Axial CT at same level showed cyst (arrow), but results were otherwise unremarkable. Criteria of Sallée et al. (5,10–13) for cyst infection were also met in this patient.

microbiologic status. In none of the cases (0/5) would this change have been beneficial for treating cyst infection.

DISCUSSION

The results of the present study show that, compared with a previously established composite clinical and biochemical reference standard (5,10–13), ^{18}F -FDG PET/CT achieved high diagnostic performance in detecting renal or hepatic cyst infection in patients with ADPKD.

Moreover, ^{18}F -FDG PET/CT detected extrarenal and extrahepatic inflammatory or infectious lesions in several cases; these results further enhance its value in the evaluation of patients with ADPKD and suspected infection. An important finding of the present study was that patients with ^{18}F -FDG PET/CT scan results who were positive for cyst infection had significantly longer total duration of hospitalization and duration between their ^{18}F -FDG PET/CT scans and hospital discharge than patients with ^{18}F -FDG PET/CT scan results that were negative for cyst infection or any other infection. This finding can be interpreted in 2 ways: the ^{18}F -FDG PET/CT scan gave clinicians confidence to discharge these patients sooner or these patients were truly in a better clinical condition that allowed earlier hospital discharge. However, clinical parameters did not differ significantly between these patients. In light of these findings, performing ^{18}F -FDG PET/CT early in such patients may reduce health care costs.

The antibiotic regimen for patients with ^{18}F -FDG PET/CT scan results that were positive for cyst infection was adapted to a regimen favorable for treating cyst infections more often than that for patients with ^{18}F -FDG PET/CT scan results that were negative for cyst infection or positive for another infection. These data indicated that patients with positive results for cyst infection were switched to or maintained on antibiotics favorable for treating cyst infection on the basis of the ^{18}F -FDG PET/CT results. Another interesting finding of the present study was that patients in whom cyst infection was suspected but in whom no cyst infection was found on ^{18}F -FDG PET/CT had significantly lower levels of creatinine in blood than patients in whom cyst infection was found.

The utility of ^{18}F -FDG PET/CT in ADPKD patients was explored in a few previous studies (5,10–15). Jouret et al. (13) included 27 ^{18}F -FDG PET/CT scans from 24 different ADPKD patients in whom abdominal infection was suspected between 2005 and 2009. Using the criteria of Sallée et al. (5) as a diagnostic reference, they found a sensitivity of 85% and a specificity of 86% for ^{18}F -FDG PET/CT in diagnosing cyst infection. However, only 11 of the 27 selected ^{18}F -FDG PET/CT scans were positive for cyst infection. In a retrospective single-center study by Balbo et al. (10), 34 episodes of suspected abdominal infection were identified in 27 ADPKD patients and 1 autosomal dominant polycystic liver disease patient between 2010 and 2012. Twenty ^{18}F -FDG PET/CT scans performed for these patients yielded a sensitivity of 95% (19/20) when the criteria of Sallée et al. were used as a reference standard (5,11–13), but no ^{18}F -FDG PET/CT scans from patients without cyst infection were included in that analysis (10). In a study by Bobot et al. (11), 32 ^{18}F -FDG PET/CT scans from 24 ADPKD patients with suspected cyst infection were retrospectively analyzed. ^{18}F -FDG PET/CT achieved a sensitivity of 77% and a specificity of 100%, according to the criteria of Sallée et al. (5,10,12,13). ^{18}F -FDG PET/CT allowed a differential diagnosis in 7 patients, supporting the role of ^{18}F -FDG PET/CT

TABLE 4
Antibiotic Regimen After ^{18}F -FDG PET/CT

^{18}F -FDG PET/CT finding	No. of patients of whom appropriate antibiotics were maintained or changed*	No. of patients of whom inappropriate antibiotics were maintained or changed†
Cyst infection ($n = 19$)	12	7
False-positive result for cyst infection‡ ($n = 3$)	1	2
No cyst infection ($n = 6$)	3	3
False-negative result for cyst infection‡ ($n = 2$)	2	0
Other infectious focus ($n = 5$)	0	5

*Maintained on or switched to lipophilic antibiotics favorable for treating cyst infections (fluoroquinolones or trimethoprim-sulfamethoxazole).

†Maintained on or switched to hydrophilic antibiotics not favorable for treating cyst infections (ceftriaxone or meropenem).

‡According to criteria of Sallée et al. (5).

in both the diagnosis of renal or hepatic cyst infection and the detection of active disease elsewhere in the body. The results of these and some smaller studies are summarized in Table 1.

The present study had some limitations. First, because of the retrospective design, there may have been selection bias. Second, as mentioned earlier, the reference standard was suboptimal but in line with that in previous studies (5,10–15). According to this reference standard, some results had to be considered false-positive or false-negative on the basis of clinical parameters, despite signs of infection on ^{18}F -FDG PET/CT imaging. Therefore, whether these results were truly false-positive or false-negative remains questionable. Cyst aspiration was not performed in any of the patients, and follow-up ^{18}F -FDG PET/CT scans were not available. Third, other cross-sectional imaging modalities, such as ultrasound, CT, or MRI, were available only in a relatively small number of cases. Bobot et al. (11) had already reported CT to be significantly inferior ($P < 0.001$) to ^{18}F -FDG PET/CT in terms of both sensitivity (7% vs. 100%) and negative predictive value (35% vs. 77%) in this setting. How ^{18}F -FDG PET/CT performs compared with MRI is still unknown. Diffusion-weighted MRI was proposed as a potentially sensitive sequence for lesion detection, including cyst infection, because of its high lesion-to-background contrast (19). However, the specificity of this sequence is unclear because it may also yield positive results for bleeding and tumors (20). Furthermore, unlike ^{18}F -FDG PET/CT, (upper) abdominal MRI does not provide information about other body regions that may harbor inflammatory or infectious foci, and the procedure is time-consuming and not tolerated by very ill patients.

In a recent pictorial essay of our own, we discussed the potential use of ^{18}F -FDG PET/CT for diagnosing cyst infection (21). We showed 5 exemplary cases of cysts or cystlike lesions that illustrated not only the advantages but also the potential pitfalls of using ^{18}F -FDG PET/CT to diagnose cyst infection in ADPKD patients. We also briefly discussed the results of other studies investigating the performance of ^{18}F -FDG PET/CT for diagnosing cyst infection.

To our knowledge, in the present study, we report on the largest series of ADPKD patients with ^{18}F -FDG PET/CT scan results that were positive for cyst infection thus far. In addition, we believe that we are the first to report on ^{18}F -FDG PET/CT scans for a particular group of patients, and we are the first to analyze the

relationship between ^{18}F -FDG PET/CT results and the duration of a hospital stay.

Recent European Association of Nuclear Medicine guidelines still described the use of ^{18}F -FDG PET/CT for the evaluation of potentially infected liver and kidney cysts in polycystic disease patients as insufficiently evidence-based (16). These guidelines, however, were established in 2013 and were based on 7 studies reporting, in total, only 34 scans in 28 patients (21). Since then, larger studies, including our own, reported high sensitivity and specificity for ^{18}F -FDG PET/CT in diagnosing cyst infection. The total number of included patients exceeds those with diseases that are considered to be “major” indications for performing ^{18}F -FDG PET/CT, such as spondylodiskitis. Therefore, there appears to be sufficient evidence to consider a suspected cyst infection to be a major indication for performing an ^{18}F -FDG PET/CT scan.

CONCLUSION

^{18}F -FDG PET/CT is a useful imaging modality for the evaluation of patients with ADPKD and suspected cyst infection.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

REFERENCES

- Gabow PA. Autosomal dominant polycystic kidney disease. *N Engl J Med*. 1993;329:332–342.
- Hateboer N, v Dijk MA, Bogdanova N, et al. Comparison of phenotypes of polycystic kidney disease types 1 and 2. *Lancet*. 1999;353:103–107.
- Torres VE, Harris PC, Pirson Y. Autosomal dominant polycystic kidney disease. *Lancet*. 2007;369:1287–1301.
- Alam A, Perrone RD. Managing cyst infections in ADPKD: an old problem looking for new answers. *Clin J Am Soc Nephrol*. 2009;4:1154–1155.
- Sallée M, Rafat C, Zahar JR, et al. Cyst infections in patients with autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol*. 2009;4:1183–1189.
- Fick GM, Johnson AM, Hammond WS, Gabow PA. Causes of death in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol*. 1995;5:2048–2056.
- Lantinga MA, Drenth JP, Gevers TJ. Diagnostic criteria in renal and hepatic cyst infection. *Nephrol Dial Transplant*. 2015;30:744–751.

8. Jouret F, Lhommel R, Devuyt O, et al. Diagnosis of cyst infection in patients with autosomal dominant polycystic kidney disease: attributes and limitations of the current modalities. *Nephrol Dial Transplant*. 2012;27:3746–3751.
9. Vaidyanathan S, Patel CN, Scarsbrook AF, Chowdhury FU. FDG PET/CT in infection and inflammation: current and emerging clinical applications. *Clin Radiol*. 2015;70:787–800.
10. Balbo BE, Sapienza MT, Ono CR, et al. Cyst infection in hospital-admitted autosomal dominant polycystic kidney disease patients is predominantly multifocal and associated with kidney and liver volume. *Braz J Med Biol Res*. 2014;47:584–593.
11. Bobot M, Ghez C, Gondouin B, et al. Diagnostic performance of (¹⁸F)fluorodeoxyglucose positron emission tomography-computed tomography in cyst infection in patients with autosomal dominant polycystic kidney disease. *Clin Microbiol Infect*. 2016;22:71–77.
12. Neuville M, Hustinx R, Jacques J, Krzesinski JM, Jouret F. Diagnostic algorithm in the management of acute febrile abdomen in patients with autosomal dominant polycystic kidney disease. *PLoS One*. 2016;11:e0161277.
13. Jouret F, Lhommel R, Beguin C, et al. Positron-emission computed tomography in cyst infection diagnosis in patients with autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol*. 2011;6:1644–1650.
14. Piccoli GB, Arena V, Consiglio V, et al. Positron emission tomography in the diagnostic pathway for intracystic infection in ADPKD and “cystic” kidneys: a case series. *BMC Nephrol*. 2011;12:48.
15. Bleeker-Rovers CP, De Sévaux RG, Van Hamersvelt HW, Corstens FH, Oyen WJ. Diagnosis of renal and hepatic cyst infections by 18-F-fluorodeoxyglucose positron emission tomography in autosomal dominant polycystic kidney disease. *Am J Kidney Dis*. 2003;41:E18–E21.
16. Jamar F, Buscombe J, Chiti A, et al. EANM/SNMMI guideline for ¹⁸F-FDG use in inflammation and infection. *J Nucl Med*. 2013;54:647–658.
17. Pei Y, Obaji J, Dupuis A, et al. Unified criteria for ultrasonographic diagnosis of ADPKD. *J Am Soc Nephrol*. 2009;20:205–212.
18. Boellaard R, Delgado-Bolton R, Oyen WJ, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging—version 2.0. *Eur J Nucl Med Mol Imaging*. 2015;42:328–354.
19. Katano K, Kakuchi Y, Nakashima A, Takahashi S, Kawano M. Efficacy of diffusion-weighted magnetic resonance imaging in detecting infected cysts in a case of polycystic kidney disease. *Clin Nephrol*. 2011;75(suppl 1): 24–26.
20. Zeile M, Andreou D, Poellinger A, Tunn PU, Dudeck O. Identification of the primary tumour with the help of diffusion-weighted MRI in a patient with autosomal dominant polycystic kidney disease and metastatic renal cell carcinoma. *Br J Radiol*. 2011;84:e142–e145.
21. Pijl JP, Kwee TC, Slart RHJA, Glaudemans AWJM. FDG-PET/CT for diagnosis of cyst infection in autosomal dominant polycystic kidney disease. *Clin Transl Imaging*. 2018;6:61–67.



The Journal of
NUCLEAR MEDICINE

^{18}F -FDG PET/CT in Autosomal Dominant Polycystic Kidney Disease Patients with Suspected Cyst Infection

Jordy P. Pijl, Andor W.J.M. Glaudemans, Riemer H.J.A. Slart and Thomas C. Kwee

J Nucl Med. 2018;59:1734-1741.

Published online: April 13, 2018.

Doi: 10.2967/jnumed.117.199448

This article and updated information are available at:
<http://jnm.snmjournals.org/content/59/11/1734>

Information about reproducing figures, tables, or other portions of this article can be found online at:
<http://jnm.snmjournals.org/site/misc/permission.xhtml>

Information about subscriptions to JNM can be found at:
<http://jnm.snmjournals.org/site/subscriptions/online.xhtml>

The Journal of Nuclear Medicine is published monthly.
SNMMI | Society of Nuclear Medicine and Molecular Imaging
1850 Samuel Morse Drive, Reston, VA 20190.
(Print ISSN: 0161-5505, Online ISSN: 2159-662X)

© Copyright 2018 SNMMI; all rights reserved.

The logo for the Society of Nuclear Medicine and Molecular Imaging (SNMMI) consists of the letters 'S', 'N', 'M', and 'I' arranged in a 2x2 grid. Each letter is white and set within a red square. To the right of this grid, the full name of the society is written in a sans-serif font: 'SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING'.

SOCIETY OF
NUCLEAR MEDICINE
AND MOLECULAR IMAGING