

University of Groningen

Role of FDG-PET/CT in the evaluation of infectious and inflammatory disease

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DOI:
[10.33612/diss.791749362](https://doi.org/10.33612/diss.791749362)

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:
2023

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

Citation for published version (APA):

Pijl, J. (2023). *Role of FDG-PET/CT in the evaluation of infectious and inflammatory disease*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.791749362>

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CHAPTER 4

18F-FDG PET/CT in autosomal dominant polycystic kidney disease patients with suspected cyst infection

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Published in J Nucl Med (2018);6(1):61-67.

ABSTRACT

Purpose

To determine the value of 18F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET)/computed tomography (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 with ADPKD who underwent FDGPET/CT because of suspected cyst infection between 2010 and 2017.

Results

Thirty FDG-PET/CT scans of thirty individual patients were included, of which 19 were positive for cyst infection. According to a previously established clinical and biochemical reference standard, FDG-PET/CT achieved sensitivity of 88.9%, specificity of 75.0%, positive predictive value of 84.2%, and negative predictive value of 81.8% for the diagnosis of cyst infection. In 5 cases, FDG-PET/CT suggested a different pathologic process that explained the symptoms, including pneumonia (n=1), generalized peritonitis (n=1), pancreatitis (n=1), colitis (n=1), and cholangitis (n=1). Total duration of hospital stay and duration between FDG-PET/CT scan and hospital discharge of patients with an FDG-PET/CT scan positive for cyst infection were significantly longer than those with a negative scan (P=0.005 and P=0.009, respectively). Creatinine levels were significantly higher in patients with an FDGPET/CT scan positive for cyst infection than in patients with a negative scan (P=0.015). Other comparisons of clinical parameters (age, gender, presence of fever (>38.5°C) for more than 3 days, abdominal pain, history of solid organ transplantation and nephrectomy, immune status), laboratory values (C-reactive protein level (CRP), leukocyte count, estimated glomerular filtration rate), and microbiologic results (blood and urine cultures) were not significantly different (P=0.13-1.00) between FDG-PET/CT-positive and -negative patients.

Conclusion

FDG-PET/CT is a useful and recommendable (upfront) imaging modality for the evaluation of patients with ADPKD and suspected cyst infection.

INTRODUCTION

With a reported prevalence of 1 in 400 to 1000, 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 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 one renal cyst infection during their life^[4], and approximately 10% of hospitalizations in ADPKD patients are due to cyst infection^[5].

Prompt diagnosis of cyst infection is important, as cyst infections require specific treatment^[3]. Most conventional antibiotics are hydrophilic substances, which prevents them from penetrating the cystic walls with as consequence 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 to prevent 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 gold diagnostic standard, but is rarely performed due to the risk of complications such as contamination of adjacent cysts, sepsis, bleeding, or even death^[6]. Moreover, which cyst is infected is difficult to identify, and often an infected cyst cannot be accessed percutaneously^[7]. Conventional radiologic modalities such as ultrasonography, computed tomography (CT), and magnetic resonance imaging (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, due to the potential risks of nephrotoxicity and nephrogenic systemic fibrosis, respectively^[8].

¹⁸F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET), on the other hand, may be a potentially useful imaging technique to detect cyst infection. Activated inflammatory cells (such as macrophages and neutrophils) at a site of infection accumulate FDG^[9], which can be visualized by PET with a high contrast ratio and anatomically pinpointed with concomitantly acquired CT. Also, the administration of FDG does not pose any contraindication in patients with impaired renal function.

Previous studies have reported FDG-PET/CT to be useful in ADPKD^[5,10-15] (Table 1). Due to few included patients or unclear reporting of diagnostic power in these studies, there is still no consensus and widespread use of FDG-PET/CT in this setting. Recent European Association of Nuclear Medicine guidelines describe the use of FDG-PET/CT still as an insufficiently evidence-based indication for evaluation of potentially infected liver and kidney cysts in polycystic disease^[16].

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

Table 1 | Previous literature on the diagnosis of cyst infection in polycystic patients

Study	Included patients	Included scans	PET-positive cyst infections	Sensitivity	Specificity
Neuville 2016 ^a	Unknown	28	8	80% (8/10)	89% (16/18)
Bobot 2016 ^a	24	32	14	77% (14/18)	100% (14/14)
Balbo 2014 ^a	28	Unknown	19	95% (19/20)	Unknown
Piccoli 2011 ^b	10	10	6	Unknown	Unknown
Jouret 2011 ^a	24	27	11	85% (11/13)	86% (12/14)
Sallée 2009 ^a	8	8	8	100% (8/8)	Unknown
Bleeker-Rovers 2003 ^b	3	7	5	Unknown	Unknown

Notes:

^a Reference standard of Sallée et al (2009) used for confirming cyst infection found on FDG-PET/CT.

^b Other clinical criteria and follow-up used as reference standard for diagnosing cyst infection on FDG-PET/CT.

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 with ADPKD who underwent 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 FDG-PET/CT imaging that was performed to diagnose cyst infection. Exclusion criteria were: no diagnosis of ADPKD, FDG-PET/CT that was not performed because a potential cyst infection, and specific missing clinical and laboratory data. The presence of fever, abdominal pain, and CRP level were used as part of the reference standard (as will be explained in a later section), hence the results of the FDG-PET/CT scan could not be tested against the reference standard in the absence of these data. If a patient underwent multiple FDGPET/CT scans because of suspected cyst infection, the FDG-PET/CT scan first performed was selected, and the subsequent scans were excluded.

Patient Record Review

Medical records of included patients were reviewed for relevant clinical data (age, gender, presence of fever (>38.5°C) for more than 3 days, abdominal pain, history of solid organ transplantation and nephrectomy, immune status, duration of hospital stay, antibiotics use), laboratory values (C-reactive protein level (CRP), leukocyte count, creatinine level, estimated glomerular filtration rate, microbiologic tests (blood and urine cultures), and all other imaging studies that were performed during hospitalization for suspected cyst infection. All laboratory values were measured within a 2-day time frame of the FDG-PET/CT scan.

FDG-PET Acquisition

Patients fasted for a minimum of 6 hours and blood glucose concentrations were checked to be less than 11 mmol/L before 3 MBq FDG/kg body weight was administered intravenously. Approximately 60 minutes after FDG administration, PET scanning was performed from midthigh to cranial vertex using a resEARCh 4 Life (EARL)-accredited integrated PET/CT system (Biograph mCT 64 slice PET/CT, Siemens, Knoxville, TN, USA) with 3 minutes per bed position. Low-dose CT was performed for attenuation correction and anatomic mapping with 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 (Siemens CARE Dose 4D) with a quality reference effective tube current-time product of 30 mAs, an average tube current of 90 mA, 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 automatic adjustment of mAs in the z-direction, with scanning in the portal venous phase in 3 patients and without administration of intravenous contrast agent in 1 patient.

FDG-PET Interpretation

FDG-PET/CT scans were interpreted by board-certified nuclear medicine physicians as part of routine clinical care, using Syngo.Via software (Siemens Healthcare, Erlangen, Germany). Each scan was re-evaluated by another reader who was blinded to original FDG-PET/CT interpretations, other imaging, clinical, laboratory, and microbiologic tests. Renal or liver cysts with increased FDG uptake of cyst walls compared to surrounding residual parenchyma (excluding physiological urinary excretion), heterogenous FDG uptake in the cyst wall (including focal or multifocal increased uptake), or cysts with diffuse signal accumulation within the cyst after exclusion of cyst hemorrhage by CT were considered positive for infection. Extrarenal and extrahepatic organs were also evaluated for pathologic foci of FDG uptake that may represent inflammation or infection. The low-dose CT part of the 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 FDG-PET/CT reports to assess for any discrepancies.

Reference Standard

Given the lack of cyst aspiration and subsequent microbiologic testing due to previously mentioned reasons, a composite reference standard was used for cyst infection according to the previously used criteria by Sallée et al.^[5,10-13]. According to these criteria (5,10-13), hepatic or renal cyst infection was (likely) considered to be present if a patient met all of the following five criteria:

- 1 Fever of >38.5°C for >3 days
- 2 Presence of abdominal pain
- 3 CRP level >50 mg/L
- 4 Absence of any recent intracystic bleeding or other known causes of fever
- 5 Favorable outcome with antibiotic treatment

The FDG-PET/CT scans were considered as 'true positive' for cyst infection when the patients met all five criteria and the scan showed signs of cyst infection as described above. If the patients met all criteria, but their FDG-PET/CT scan did not show signs of cyst infection, the scan was considered as 'false negative'.

Statistical Analysis

Continuous variables were checked for normal distribution using Kolmogorov-Smirnov tests. Data were presented as mean \pm standard deviation or median with interquartile range for normally distributed or non-normally distributed data, respectively.

Sensitivity, specificity, positive predictive value, and negative predictive value of FDG-PET/CT for the diagnosis of hepatic and renal cyst infection were calculated, along with 95% confidence intervals (CIs). Differences in clinical parameters (age, gender, presence of fever ($>38.5^{\circ}\text{C}$) for more than 3 days, abdominal pain, history of solid organ transplantation and nephrectomy, immune status, duration of hospital stay), laboratory values (CRP level, leukocyte count, creatinine level, estimated glomerular filtration rate), and microbiologic tests (blood and urine cultures) between FDG-PET/CT-positive and -negative cases for hepatic or renal cyst infection (excluding patients with FDG-avid foci elsewhere), and between all FDG-PET/CT-positive and -negative cases (also including patients with FDG-avid foci outside the liver and kidneys), were assessed using two-tailed unpaired t-tests for normally distributed data, Mann-Whitney tests for non-normally distributed data, and Fisher tests for dichotomous data. P-values less than 0.05 were considered statistically significant.

Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) version 25 (SPSS, Chicago, IL, USA).

RESULTS

FDG-PET/CT Scans and Patients

Sixty-seven FDG-PET/CT scans were potentially eligible for inclusion, however 21 were excluded because they did not fulfill the criteria for ADPKD, 11 FDG-PET/CT scans were excluded because they belonged to a patient of whom a previous scan had already been included, and 5 FDG-PET/CT scans were excluded because of missing clinical, laboratory, and microbiologic data due to transfer to another hospital. Finally, 30 FDG-PET/CT scans in 30 individual patients were included. These 30 scans were performed in 15 men and 15 women, with a median age of 61 years (Table 2). Most FDG-PET/CT scans were performed in patients with a solid organ transplant (20/30, 67%), the majority of patients were immunocompromised (26/30, 87%), and most patients had a positive blood or urine culture (22/30, 73%) (Table 3). The mean duration of hospital stay was 12.6 days.

Main FDG-PET/CT Findings

In 24 out of 30 cases (80%), a focus of infection was identified on the FDG-PET/CT scan. These 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 FDG-PET/CT led to or confirmed the main clinical diagnosis of the patient. In the remaining 6 negative FDG-PET/CT cases, the final 'diagnoses' were urinary tract infection (n=3, based on positive urine cultures), fever of unknown origin (n=2, based on the lack of any positive test results) and urosepsis (n=1, based on blood cultures).

Table 2 | Clinical parameters of all included patients and comparison between FDG-PET/CT-positive and -negative patients.

Parameter	All patients (n=30)	Any infectious focus found on FDG-PET/CT (n=24)	No infectious focus found on FDG-PET/CT (n=6)	Cyst infection found on FDG-PET/CT (n=19) ^a	Any infectious focus vs. no infectious focus found on FDG-PET/CT	FDG-PET/CT cyst positive vs. negative patients
Age (y)	61.0 (9.0) ^c	61.5 (11.0) ^c	60.0 (7.0) ^c	57.5 (10.0) ^c	.516 ^e	0.975 ^e
Gender (M/F)	15/15	11/13	4/2	7/12	.651 ^f	0.35 ^f
Presence of fever (>38.5°C) for >3 days (yes/no)	26/4	21/3	5/1	17/2	1.0 ^f	1.0 ^f
Presence of abdominal pain (yes/no)	25/5	20/4	5/1	17/2	1.0 ^f	1.0 ^f
Solid organ transplant (yes/no)	20/10	14/10	6/0	10/9	0.074 ^f	0.057 ^f
-Kidney	17	14	6	10		
-Liver	2	1	1	0		
Nephrectomy performed	9	8	1	7	0.633 ^f	0.624 ^f
-Unilateral	6	6	0	6		
-Bilateral	3	2	1	1		
Immunocompromised (yes/no)	26/4	20/4	6/0	15/4	0.557 ^f	0.54 ^f
-Use of immunosuppressants	20	14	6	10		
-Dialysis	6	6	0	5		
Duration hospital stay (days)						
-Total						
-between admission and PET/CT scan	12.6 ± 10.2 ^b , 4.89 ± 4.0 ^b ,	14.3 ± 10.9 ^{b,§} , 5.5 ± 4.4 ^{b,§}	6.3 ± 1.5 ^b , 3.7 ± 1.8 ^b	15.2 ± 11.6 ^{b,h} , 5.1 ± 4.3 ^{b,h}	0.003 ^d , 0.201 ^d	0.005 ^d , 0.256 ^d
- between PET/CT scan and discharge	7.7 ± 9.0 ^b ,	9.1 ± 9.7 ^{b,§}	2.7 ± 1.9 ^b	10.1 ± 10.4 ^{b,h}	0.122 ^d	0.009 ^d

Notes:

^a Of whom 11 with an FDG-avid renal cyst and 8 with an FDG-avid hepatic cyst

^b Mean ± SD

^c Median with IQR between parentheses

^d P-value unpaired t-test

^e P-value Mann-Whitney test

^f P-value Fisher test

^g Only 22 out of 24 FDG-PET/CT scans positive for cyst infection were included (2 scans were performed after hospital discharge)

^h Only 18 out of 19 FDG-PET/CT scans positive for cyst infection were included (1 scan was performed after hospital discharge)

Table 3 | Laboratory values of all included patients and comparison between FDG-PET/CT-positive and -negative patients.

Parameter	All patients (n=30)	Any infectious focus found on FDG-PET/CT (n=24)	No infectious focus found on FDG-PET/CT (n=6)	Cyst infection found on FDG-PET/CT (n=19) ^a	Any infectious focus vs. no infectious focus found on FDG-PET/CT	FDG-PET/CT cyst positive vs. negative patients
CRP (mg/dL)	95 (82) ^c	106 (95) ^c	109 (66) ^c	106 (91) ^c	.917 ^e	.899 ^e
CRP >50 (yes/no)	29/1	23/1	6/0	18/1	1.0 ^f	1.0 ^f
Leukocyte count (g/L)	8.9 (5.3) ^c	8.9 (7.5) ^c	9.0 (4.6) ^c	8.9 (8.4) ^c	.659 ^e	.702 ^e
Creatinine (umol/L)	253 ± 246 ^b	283 ± 264 ^b	121 ± 52 ^b	307 ± 282 ^b	0.011 ^d	0.015 ^d
eGFR (mL/min/1.73m2) ^g	48 (45) ^c	40 (51) ^c	55 (37) ^c	35 (51) ^c	.144 ^e	.125 ^e
Positive blood culture (yes/no)	12/18	8/16	4/2	6/13	.184 ^f	0.175 ^f
-E. coli	5	3	2			
-E. faecalis	2	2	0			
-Other	5	3	2			
Positive urine culture (yes/no)	17/13	14/10	3/3	13/6	1.0 ^f	0.630 ^f
-E. coli	8	6	2			
-K. pneumoniae	4	4	0			
-Other	5	4	1			

Notes:

^a Of whom 11 with an FDG-avid renal cyst and 8 with an FDG-avid hepatic cyst

^b Mean ± SD

^c Median with IQR between parentheses

^d P-value unpaired t-test

^e P-value Mann-Whitney test

^f P-value Fisher test

^g eGFR: estimated glomerular filtration rate

Diagnostic Performance FDG-PET/CT

Nineteen out of 30 FDG-PET/CT scans (63%) were judged positive for cyst infection (of which 11 renal cyst infections and 8 hepatic cyst infections), with no discrepancies between the original reports and the re-evaluation. There were no cases with intracystic bleeding. According to the reference standard, FDG-PET/CT provided 16 true-positives, 3 false-positives (due to lack of abdominal pain or fever), 9 true-negatives, and 2 falsenegatives for cyst infection. This resulted in sensitivity of 88.9% (95% CI: 65.3-98.6%), specificity of 75.0% (95% CI: 42.8-94.5%), positive predictive value of 84.2% (95% CI: 66.4-93.5%), and negative predictive value of 81.8% (95% CI: 53.9-94.5%) for FDG-PET/CT in the diagnosis of cyst infection in ADPKD. Representative examples are shown in **Figures 1** and **2**.

In 5 out of 30 FDG-PET/CT scans, an infectious focus other than cyst infection was identified. A case of cholangitis was found on FDG-PET/CT, which was confirmed by magnetic resonance

cholangiopancreatography, Endoscopic Retrograde Cholangio-Pancreatography and clinical suspicion. In another patient, pancreatitis was found on FDG-PET/CT which was confirmed by Endoscopic Retrograde Cholangio-Pancreatography, MRI and laboratory values (markedly increased serum amylase and lipase levels). The case of pneumonia was confirmed by a chest X-ray, colitis in another patient was confirmed by microbiologic cultures and clinical findings, and the generalized peritonitis in yet another patient was confirmed by laparotomy. Including these five true-positive results, FDG-PET/CT achieved an overall sensitivity of 91.3% (95% CI: 72.0-98.9%) and a positive predictive value of 87.5% (74.7-94.3%).

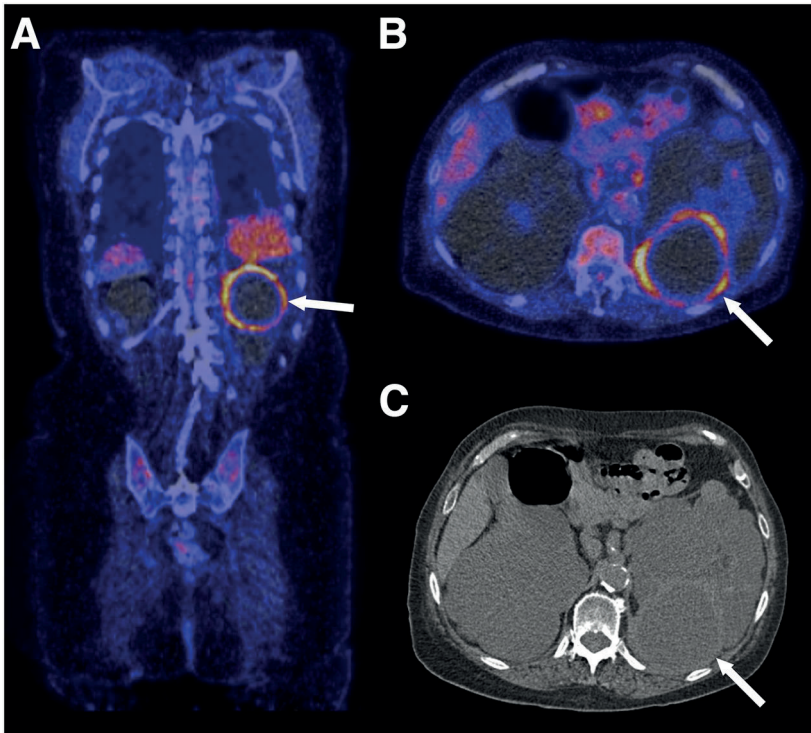


Figure 1 |

A 79-year-old woman with ADPKD in whom FDG-PET/CT was positive for renal cyst infection. Coronal (A) and axial (B) fused FDG-PET/CT shown an FDG-avid cyst wall in the left kidney (arrows), indicative of infection. Axial CT at the same level show the cyst (arrow) with slightly thickened and hyperattenuating wall. The criteria for cyst infection according to Sallée et al. ^[5,10-13] were also met in this patient.

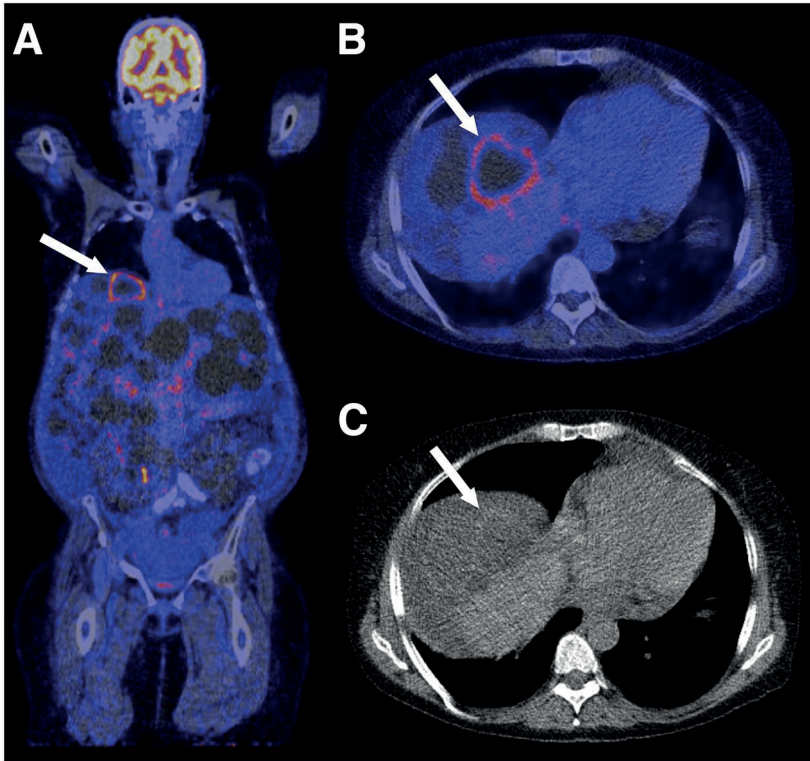


Figure 2 |

A 56-year-old woman with ADPKD in whom FDG-PET/CT was positive for hepatic cyst infection. Coronal (A) and axial (B) fused FDG-PET/CT show an FDG-avid cyst wall in liver segment 8 (arrows), indicative of infection. Axial CT at the same level shows the cyst (arrow), but is otherwise unremarkable. The criteria for cyst infection according to Sallée et al.^[5,10-13] were also met in this patient.

Alternative Imaging for Cyst Infection

Around the time of the FDG-PET/CT scan, abdominal ultrasonography was performed in 8 patients, full dose contrast-enhanced CT in 4 patients, and MRI in 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 provided 1 true-negative and 3 false-negative results, and MRI 2 true-negative results.

FDG-PET/CT Status vs. Clinical, Laboratory, and Microbiologic Parameters Various clinical, laboratory and microbiologic data are summarized in Tables 2 and 3.

Interestingly, total duration of hospital stay and duration between the FDG-PET/CT scan and discharge from hospital of patients with a positive FDG-PET/CT scan were significantly longer

($P=0.005$ and $P=0.009$, respectively) than those with a negative FDG-PET/CT-scan. Creatinine levels were significantly higher ($P=0.015$) in patients with an FDG-PET/CT scan positive for cyst infection. All other comparisons of clinical, laboratory, and microbiologic parameters were not significantly different ($P=0.13-1.00$) between FDG-PET/CT-positive and -negative patients.

Antibiotics Use

After FDG-PET/CT, the antibiotic regimen of patients with a cyst infection according to FDG-PET/CT was maintained on or changed to antibiotics favorable for treating cyst infection in 63% of patients (12/19) (Table 4). In patients in whom no infection was found on FDG-PET/CT, this was done in 50% (3/6). When an infection focus other than cyst infection was found on FDG-PET/CT, antibiotic therapy was switched to the better option according to clinical and microbiological status. In none of the cases (0/5), this change would have been beneficial for treating cyst infection.

Table 4 | Antibiotic regimen after FDG-PET/CT.

FDG-PET/CT finding	Patients changed to or maintained on appropriate antibiotics ^a	Patients changed to or maintained on inappropriate antibiotics ^b
Cyst infection (n=19)	12	7
False positive for cyst infection ^c (n=3)	1	2
No cyst infection (n=6)	3	3
False negative for cyst infection ^c (n=2)	2	0
Other infectious focus (n=5)	0	5

Notes:

^a Maintained on or switched to lipophilic antibiotics in favor of treating cyst infections (fluoroquinolones or trimethoprim-sulfamethoxazole)

^b Maintained on or switched to hydrophilic antibiotics not favorable for treating cyst infections (i.e. ceftriaxone, meropenem)

^c According to the criteria of Sallée et al (2009).

DISCUSSION

The results of this study show that FDG-PET/CT achieves a high diagnostic performance in detecting renal or hepatic cyst infection in patients with ADPKD, when compared to a previously established composite clinical and biochemical reference standard^[5,10-13].

Moreover, FDG-PET/CT detected extrarenal and extrahepatic inflammatory or infectious lesions in several cases, which further enhances its value in the evaluation of patients with ADPKD and suspected infection. An important finding of this study was that patients with an FDG-PET/CT scan positive for cyst infection had a significantly longer total duration of hospitalization and duration between their FDG-PET/CT scan and hospital discharge than patients with an FDG-PET/CT scan that was negative for cyst infection or any other infection. This can be interpreted in two ways: the FDG-PET/CT scan gave clinicians confidence to discharge these patients sooner, or these patients were truly in a better clinical condition which allowed sooner hospital discharge. However, clinical parameters did not differ significantly between these patients. In light of these findings it can be speculated to perform FDG-PET/CT early on in these patients to reduce healthcare costs.

The antibiotic regimen of patients with an FDG-PET/CT scan that was positive for cyst infection was also adapted to a regimen favorable for treating cyst infections more often than in patients with an FDG-PET/CT scan negative for cyst infection or positive for another infection. This indicates that patients positive for cyst infection were switched to or maintained on antibiotics favorable for treating cyst infection based on FDG-PET/CT results.

Another interesting finding of this study was that patients suspected of having a cyst infection but in whom no cyst infection was found on FDG-PET/CT, had significantly lower blood levels of creatinine than patients in whom a cyst infection was found.

A few previous studies have explored the utility of FDG-PET/CT in ADPKD^[5,10-15].

A study by Jouret et al.^[13] included 27 FDG-PET/CT scans from 24 different ADPKD patients suspected of abdominal infection between 2005 and 2009. Using the Sallée criteria as diagnostic reference, they found a sensitivity of 85% and a specificity of 86% for FDG-PET/CT in diagnosing cyst infection. However, only 11 out of the 27 selected FDG-PET/CT scans were positive for cyst infection. In another 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 FDGPET/CT scans were performed in these patients, which yielded a sensitivity of 95% (19/20) using the Sallée criteria as reference standard^[5,11-13], but no FDG-PET/CT scans without cyst infection were included in this analysis^[10]. In another retrospective study by Bobot et al.^[11], 32 FDG-PET/CT scans of 24 ADPKD patients with suspected cyst infection were retrospectively analyzed. FDG-PET/CT achieved a sensitivity and specificity of 77% and 100% respectively, according to the Sallée criteria^[5,10,12,13]. FDG-PET/CT allowed a differential diagnosis in seven patients, supporting the role of FDG-PET/CT for both diagnosis of renal or hepatic cyst infection and including detection of active disease elsewhere in the body. The results of these and some smaller studies are summarized in Table 1.

The current study was accompanied by some limitations. First, due to the retrospective design, there may have been selection bias. Second, as mentioned previously, the reference standard was suboptimal, but in line with previous studies^[5,10-15].

According to this reference standard, some cases had to be considered false-positives or false-negatives based on clinical parameters, despite signs of infection on FDG-PET/CT imaging. Therefore, it remains questionable whether these cases were truly false-positive or false-negative. Cyst aspiration was not performed in any of the patients, and follow-up FDGPET/CT scans were not available. Third, other cross-sectional imaging modalities such as ultrasound, CT or MRI were only available in a relatively low number of cases. The study by Bobot et al.^[11] already reported CT to be significantly inferior ($P < 0.001$) to FDG-PET/CT both in terms of sensitivity (7% vs. 100%) and negative predictive value (35% vs. 77%) in this setting. It is still unknown how FDG-PET/CT performs compared to MRI. Of interest, diffusion-weighted MRI has been proposed as a potentially sensitive sequence due to its high lesion-to-background contrast-for-lesion detection, including cyst infection^[19].

However, the specificity of this sequence is unclear, since it may also be positive in case of bleeding and tumors^[20]. Furthermore, unlike 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 already discussed the potential use of FDGPET/CT for diagnosing cyst infection^[21]. We showed five exemplary cases of cysts or cystlike lesions that not only illustrate the advantages, but also the potential pitfalls of using FDG-PET/CT to diagnose cyst infection in ADPKD. We also briefly discussed the results of other studies investigating the diagnostic performance of FDG-PET/CT for diagnosing cyst infection.

In this current study, we present the largest series of ADPKD patients with an FDGPET/CT scan positive for cyst infection thus far. We are the first to present FDG-PET/CT scans of unique patients only, and we are the first to analyze the relation between FDG-PET/CT results and duration of hospital stay.

Recent European Association of Nuclear Medicine guidelines describe the use of FDGPET/CT still as an insufficiently evidence-based indication for evaluation of potentially infected liver and kidney cysts in polycystic disease^[16]. These guidelines, however, were established in 2013 based on 7 studies reporting in total only 34 scans in 28 patients^[21].

Since then, larger studies including our own have reported a high sensitivity and specificity for FDG-PET/CT in diagnosing cyst infections. The total number of included patients exceeds evidence for diseases that are considered as 'major' indication for performing FDG-PET/CT, such as spondylodiscitis. Therefore, there appears to be sufficient evidence to consider a suspected cyst infection as a 'major' indication for performing an FDG-PET/CT scan.

CONCLUSION

FDG-PET/CT is a useful and recommendable (upfront) imaging modality for the evaluation of patients with ADPKD and suspected cyst infection.

ACKNOWLEDGEMENTS

Funding

No funding was received for this study.

Conflicts of Interest

All authors declare they have no conflicts of interest.

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